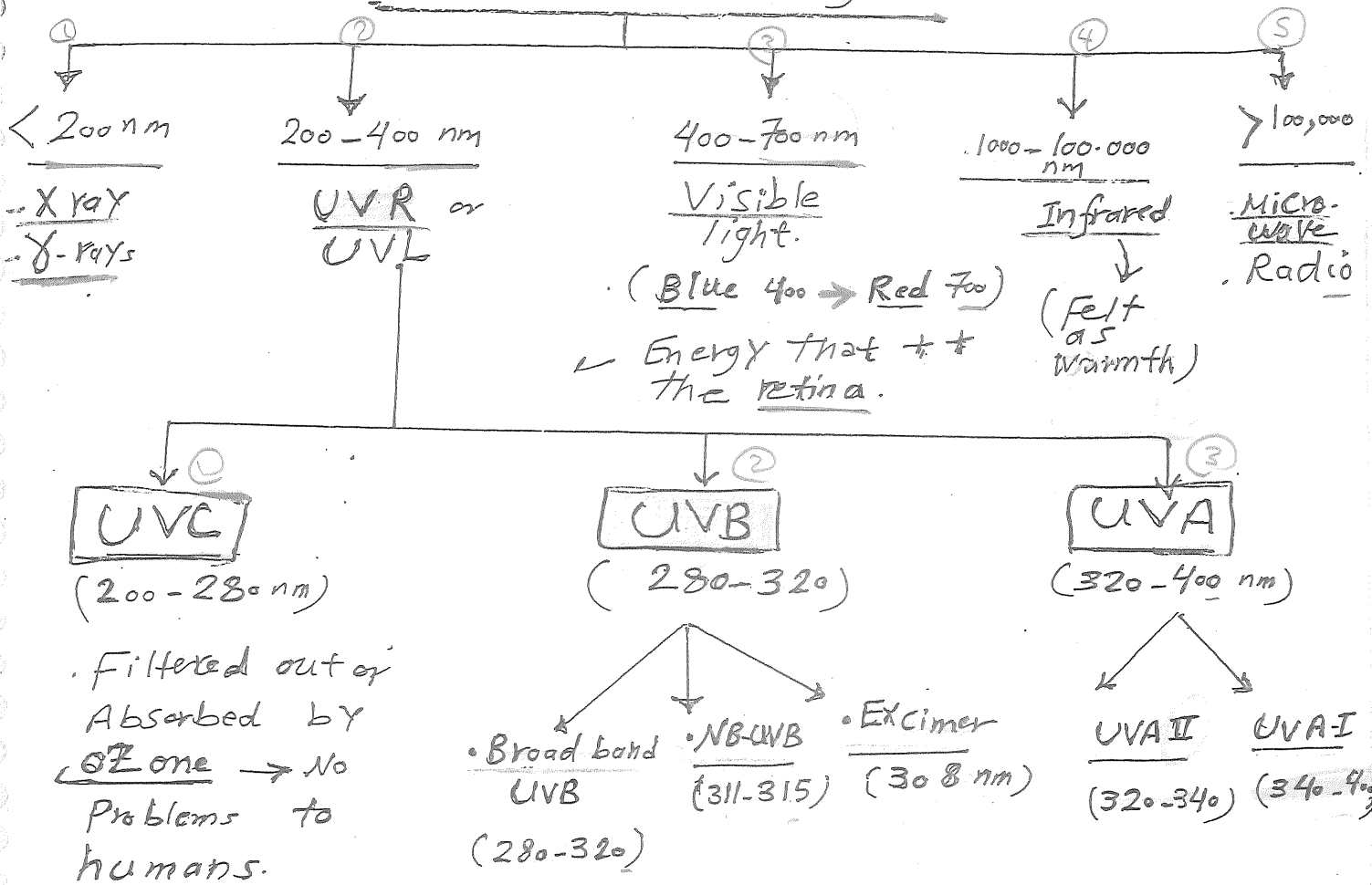


Light & Skin

(13) *of 15*

Sun. Radiation Spectrum According to the Wave length:



UVA	UVB
<ul style="list-style-type: none"> 320 - 400 nm (5%) of UVRs (0.5% of spectrum) → طوال السنة و طوال اليوم بنفس الكمية Greater in Amount (100 times > UVB) but 1000 times less potent (Erythemogenic) Penetrates deeply (Dermis & SC) 	<ul style="list-style-type: none"> 280 - 320 nm (95%) of UVR (5% of Rad. Spectrum) Maximum at 4th - 7th month of year, at 9 am - 4 pm. less in amount but more Erythemogenic. doesn't penetrate the dermis (90% Absorbed by epid.).

UVA	UVB
<p><u>Cut. effects:</u></p> <p>(1) Indirect DNA damage by releasing ROS \rightarrow less Carcinogenic</p> <p>(2) Breaks Vit D \downarrow</p> <p>(3) No Epidermal Hyperplasia \rightarrow No significant photoprotection</p> <p>(4) Immunomodulation</p>	<p>(1) Direct damage of DNA by formation of pyrimidine dimers</p> <p>(2) ++ Vit D Synth.</p> <p>(3) ++ epid. Hyperplasia & Hyperkeratosis \rightarrow Photoprotection (Hardening)</p> <p>(4) Immunomodulation</p>
"Skin diseases"	
<p>(1) Photoageing</p> <p>(2) Photosensitivity (all diseases except CAD) UVB > UVA</p> <p>(3) Darkening</p>	<p>(1) Burn</p> <p>(2) Cancer</p> <p>(3) Tanning</p>

• NB:

- Window glass blocks UVB only (< 320)
- The more the skin hydrate \rightarrow \downarrow flexion & \uparrow Absorption \rightarrow Burn.

UVB is More Carcinogenic > UVA ?? \rightarrow direct DNA damage
 90% of UVB Absorbed by epid. & most Cut. Cancers are epidermal.

Natural sun protective Mechanisms:

1. epid. thickness
2. Natural Antioxidants
3. Melanin
4. Urocanic acid
5. DNA Repair Mechanisms.

Fitzpatrick Skin Types and Recommended Sunscreen Sun Protection Factor (SPF) Levels

Skin Type	Description	Skin Color	Routine SPF	SPF for Outdoor Activity
I	Burns easily, never tans	Very fair	15	25-30
II	Burns easily, tans lightly	Fair	12-15	25-30
III	Burns somewhat, tans readily	Olive	8-10	15
IV	Burns minimally, tans well	Light brown	6-8	15
V	Doesn't burn, tans deeply (Indians)	Dark Brown	6-8	15
VI	Rarely burns, always tans	Black	6-8	15

For this analysis, the global population was broken down into three broad skin pigmentation groups, as there are insufficient data to separately quantify skin types I to IV:

- 1- Lightly pigmented – this includes skin types I to IV
- 2- Intermediate pigmentation – skin type V
- 3- Deeply pigmented – skin type VI

Cut Effects of UVR

- 1- Beneficial Effects → Vit. D synthesis.
Sense of well being.
- 2- Adverse Effects.

Aging
Burn
Cancer
Darkening & Tanning
Photosensitivity

At of some skin dis.
(vitiligo & AD)

NB: Effects may be classified as: Acute, subacute, chronic

Effects

A - Acute:

1. Sunburn
2. Pigm & Darkening
3. Epid. Hyperplasia
4. Immunological

++ Immunity ↑↑

- IL, IL6, TNFα
- AMP

-- Immunity

- [↓ LCs] ^{lose}
- [↓ funct- of LCs] ^{inhib}
- [↑ IL10]
- [↓ α MSH] } Both -- Immune
- ++ Treg

5. Repair

- NER
- Base ER
- ReCombi at- Repair
- Translational DNA Synth.

B - Chronic

1- Aging

الشيخوخة

2 Types

Intrinsic: d-t Senescence (unpreventable)

Extrinsic: d-t UVR & Smoking (photoaging = Dermato-Heliosis).

TABLE 57-1 AGE-RELATED CHANGES IN THE SKIN

Intrinsic Aging	Extrinsic Aging (Primarily UV Light)
Decrease in corneocyte adhesion	Altered keratinocyte maturation (xerosis)
Slight decrease in epidermal thickness with flattening of rete pegs	Freckles (ephelides) = lentigo senilis = liver spot
Decreased number of eccrine sweat glands	Solar lentigo
Decreased numbers of hair follicles	Guttate hypomelanosis
Canities (gray hair)	Wrinkling
Thinning and ridging of nails	Elastosis (yellowish skin)
Decreased dermal collagen (decreases 1% per year)	Telangiectasia
Decreased number of dermal elastic fibers	Senile purpura
Decreased dermal ground substance	Venous lakes
Loss or increase in subcutaneous fat (site-dependent)	Comedones = Favre Rouchet synd.

Solar < lentigo
 Senile < Elastosis
 < Purpura
 < Comedones
 < dypigm.
 < Telangiect.
 < Wrinkling, Xerosis
 < Venous lake
 < Comedones
 < Colloid Milium
 < Pseudoscars
 < Porikiloderma of Civatte
 ↓ (sparing ant. Neck)
 Vascular
 Laser jobs

Some Manifs. of Aging

< dypigm < Hyperpigim. (Hemosiderosis & purpura)
 < Hypo-pigm.

< Solar (senile) Lentigenes (difference bet. CS & CS)
 < Freckles & Lentigenes

Some Specific Patterns:

1- Solar (Actinic) Elastosis: Yellowish

Yellow Trans + Papulo striated beaded.

Translucent Papules & plaques on Neck

& striated beaded lines (Sebacous)

(Hyperplasia).

2. Solar Elastomas & Elastotic Nodules

& Fabs: Yellowish papules Resemble BCC.

3. Senile (Actinic) purpura: dorsum of hand

& forearm of Elderly → unresolved Hyperpigim.

4. Farmer's Neck (Cutis Rhomboidalis Nuchae)

5. Favre-Racouchet Synd:

- Elderly
- at Zygomatic bone & infra orbital
- 3 $\left\{ \begin{array}{l} \text{Cysts} \\ \text{Comedones} \\ \text{Elastosis} \end{array} \right.$

6. Stellate pseudoscars: d₂ like of support of Bl. vs
d₂ Collagen destruction

HL → Colloid Milium

کولائی (میلیم) (نوع)

Condition char BY:

Waxy.

① Multiple dome shaped Translucent Amber flesh colored papules on sun exposed Areas.

② dermal Colloid Material on Mic. Exam.

Variants: [1- Adult onset.
2- Juvenile H

[3- Nodular
4- Pigmented

Pathophysiology $\left\{ \begin{array}{l} \text{Et :-} \\ \text{Source :-} \end{array} \right.$

degenerative Condition linked to ③:

(i). Genetic (Inherited): Juvenile type

(ii). Sun exposure

(iii). chemicals: petrolatum & Hydroquinone

نوع

origin of Colloid deposition in Dermis: unknown but ±

• degeneration of Elastic fibers in adult form. (or fibroblasts)

• " " UV-Transformed KCs in Juvenile Form

Cause:

• Adult → Excess sun

• Juvenile → inherited susceptibility to UVR

Clinically

• lesion ± papular nodular plaques waxy, Translucent, Amber-yellow (except in pigmented type)

نوع

expressed

Lesions on side of Face & Ipsilat. Forearm → described in "Taxi Cab driver" "تاكسي كابر" (Taxis)

Hydroquinone → pigmented Colloid Milium Sometimes in ass. \bar{e} ochronosis.

Juvenile type \pm ass. \bar{e} . Ligneous conjunctivitis or Periodontitis.

Histopath. Colloid material: intradermal, amorphous, fissured, Eosinophilic material in dermis.

similar to Amyloid in histopath & histochemistry but differs in EIM

to diff bet juvenile & adult types

in it \rightarrow apoptotic KCs over the Material

(NL) KCs

- ## ① dermalabrasion, cryo, diathermy, Laser
② VitC + Exfoliating agents.

Sunburn & Solar Erythema

بش

لاز ديس نل irreversable pigm

Def. NE. cut. Reaction to sunlight in excess of an erythema dose = 4 SED on unacclimated white skin

Sunlight Exposure: onset 6 hrs
Peak 12-24 hrs (peak level of NO)

Sunburn

1w

desqua-
mation

Usually d.t. UVB by direct VD or PG Mediated IL1 & TNF

- Erythema
- Edema
- Tenderness
- \pm blistering
- \pm Constitutional manif. \leftarrow Fever, chill, Hypertension

once Redness & other symptoms appear \rightarrow ## become of limited efficacy (as the inflamm. cascade & damage is done)

PGE is important mediators so:

- Aspirin
- NSAIDs e.g. Indomethacin
- Topical Cs & Soothing agents. (Dermovate & Calamine lot)

• Pigment Darkening & Delayed tanning

Darkening
Tanning

after UVR exposure
there are 2 Responses

- onset-
- duration
- Et
- Photo protection.

* Pigment darkening (PD)

Immediate, Transient, "Grayish" pigmentation that occurs immediately following exposure & Lasts for:

- 10-20 mins (immediate PD; IPD)
- upto 12 hrs (persistent PD; PPD)

* d.t: Oxidation & Redistribution of Existing Melanin.

* UVA: induced.

* Not Photoprotective.

* Delayed Tanning

- Maximum in 2-3ds & Lasts for = 1-2 wks

* d.t: True Melanogenesis

* UVB induced:

* photoprotective against sunburn. (d.t Epid. Hyperplasia)

UVB ± UVA
Immuno suppression: UVR exposure → -- CMI (Alter LC activity, ++ product, ++ suppression TC, ++ cytokines)
Epid. Hyperplasia: (UVB)(UVC) UVR → Epid. dermal St. Corneum Hyperplasia → ± Photo protective against sunburn

• UVR & Cancer

- BCC
- SCC
- MM

Another Classification

- Immunosuppression
- Epid. Hyperplasia
- Vit-D synth.
- Others
 - Photomycobacteriosis
 - mid-dermal elastolysis

سؤال إجابتي

Ⓐ Acute & Subacute Effects

- Burn
- Darkening
- Tanning
- Photosensitivity

Ⓑ Chr. Effects

- photoaging & photocarcinogenesis

Cause of photosensitivity and photodermatoses

all UVA > UVB

Except:

1. CAD
2. SLE

Photosensitivity occurs for a variety of reasons. These can be classified into the following groups:

Photodermatoses

Causes

Idiopathic (Probably immunologically mediated)

Cause is unknown but exposure to UV light produces a clearly defined disease entity. These include:

- Polymorphic light eruption PMLE
 - Juvenile spring eruption
 - Actinic prurigo
 - Solar urticaria
 - Chronic actinic dermatitis (Actinic reticuloid)
 - Hydroa vacciniforme
 - Pseudoporphyria
 - Brachioradial Pruritus
- 2 - Solar urticaria
Pseudoporphyria

Genetic

نادر في الأطفال

photosensitive dermatoses in children

Photosensitivity is caused by a pre-existing genetic disorder, e.g.:

- Bloom syndrome
- Rothmund Thomson syndrome
- Cockayne syndrome متلازمة كوكاي
- Xeroderma pigmentosum
- Hartnup disease • PIBIDS

Metabolic

Photosensitivity is caused by a metabolic defect or imbalance of a body chemical. The most common disorders of this type are porphyrias, in which there are increased porphyrins in the skin. e.g. Porphyria

Exogenous (Drug-Induced Photosensitivity)

Photosensitivity is caused by the introduction of an external agent that is applied topically or administered internally. These agents are called photosensitisers (see Drug-Induced Photosensitivity) .. اتكلم عنها بالتفصيل

Photoexacerbated dermatoses

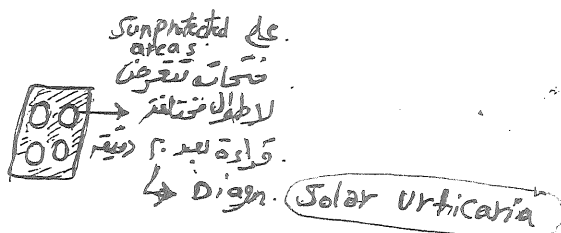
Photosensitivity is caused by a pre-existing disease or skin. These include conditions such as:

- [• Acne
- [• Atopic dermatitis AD
- [• Dermatomyositis DM
- [• Darier
- EM.
- [• GA
- [• Grovers disease
- Hailey-hailey
- [• LE
- [• LP
- [• Pellagra
- [• PRP
- [• Psoriasis, Pemphigus (Foliaceus), Rosacea, SD

NB: Although most people with the common skin conditions, psoriasis and atopic dermatitis (eczema) find sun exposure or ultraviolet light treatment helpful, about 10% report they cause flare-ups.

Lab Invs of photosensitivity:-

- HP
- ANA
- Anti Ro / Anti La
- porphyrins
- phototest →
- Photopatch test
- infants & children → Urinary Amino acids



Poly morphous Light Eruption (PMLE)

Def Acq. Idiopathic photo dermatosis
(Photo dermatosis)

Commonest

Pathophysiology

→ unknown but = Immunologically Mediated
by Type IV Hypersensitivity Reaction. in
Response to UVL (UVA, B) [but UVA > UVB]
[rarely visible]

Epidemiology

- More in females : 2:1
- More in skin types: I & II

[+ve] FH in 10-50%

[+ve] ANA in 10-20% (photosensitive SLE may give
history of PLE like eruptions for yrs. before SLE
diagnosed.. so all cases of PMLE should be
Followed up for development of SLE). "EIS"

Clinically :-

Sun exposure

4hrs

onset: 1-4 days.
Resolution: days.

4 main Eruption (Poly morphic) (pruritic)
Papular
Papulo Vesicular
Diffuse erythema
Plaque (on PLE seen)

May have several
Morphologies but in
any 1 patient only one
clinically form is
Consistently manifested.

1. Papular (Commonest)
2. Papulo Vesicular
3. Eczematous
4. plaque like (LE like) (Fixed Erythema scaly)
5. Pin point papular (Lichenitidus like)
6. pruritus only (PLE sine Eruption.)

Lateran → Eruption.

8 Juvenile Spring Eruption.

9. Generalized

1/2 - several hrs needed
for development.

"change" in amount of
is more important than
absolute amount. "ayr"

in spring (rare in Winter) or early summer
appear in summer d.t Phenom.
of "skin Hardening"

start at onset of vacation
in sunny places & ↓ E
Return to home.

Areas affected : usually sunexposed areas that's always protected from UVL during winter months e.g. Extensor forearms & chest; White < face dorsal Hands → Least affected (skin hardening)

الامكانات اللربانت متغيرة
عالمنا

→ improvement in summer & Autumn.

Juvenile Spring Eruption : - Boy Papulovesic at Helices.

- Age: Boys 5-12 (but ± Young Adults)
- Included d.t. exposure (for) sunny days during cold seasons.
- papules or papulo vesicles on helices.

- child ears

DD : L.E (more chr. vs. ms, Non-pruritic)
photosensitive drug Eruption
prurigo Nodularis.
Solar Urticaria (more)

EPP (Painful)

Diagnosis:

- (1) Clinical → sufficient
- (2) Lab : ANA → to exclude SLE
Urinary & stool porphyrins → to exclude PCT
- (3) Provocative test : exposure to UVA or UVB (phototest) → lesion → Biopsy.

- (4) HP : Dermis : Patchy dermal infilt. → Interstitial Periapillary perivascular
upper papillary dermal Edema ± Neut.
Epid. Spongiosis.

فوق

٣. حاجات

٢. LE

١. معاملة المريض

٤. مع

٥. مكان

٦. علاج

٧. الضم

Treatment:-

1- Sunprotect Program: يكتب بالظلم

2- Medications

Topical: Cs

Systemic: Cs, Antihistamines & Azathioprine or Antimalarial.

(to maintain Hardening) أ. في الربيع - أ. في الخريف - أ. في الصيف - أ. في الشتاء

3- Phototherapy: prophylactic during (Spring) to produce skin hardening.

+
Cs

→ UVA or UVB

Systemic Cs: (+) Needed to prevent Eruption during phototherapy.

Actinic Prurigo

(Hutchinson's summer prurigo)

May be variant of PMLE; AET. may be:

- ① photosensitive disorder to UVA & UVB
- ② Immunologically mediated Genetic dis.
- ③ Persistent Variant of PLE

* Age: → more common in children. (10 yrs). (F > M)

* Clinically: (1) Severely pruritic:

(AD or Acute PLE like)

- papules
- nodules
- papulovesicles

(2) ECZematizat

Hyic crustat

Lichenificat

(3) linear &

Pitted

flat scars

& dyspigment.

Other

(4) Ass. c: 4 Conjunctivitis & cheilitis

Pseudomadarosis (d.f)

- Site: sun exposed then → sun protected areas.
- Course: chronic, persistent through childhood, but often fade in Adolescence.
- Persistent throughout (Year) & exacerbate in Spring & Summer.

- HP: Acanthosis
 ↳ Spangiosis
 ↳ Dermal Edema
 ↳ Lichenification

- DD: Nodular prurigo, Photosensitive AD, EPP, Scabies, PMLE, photo CD

- III 1. as PMLE
- 2. Thalidomide showed to be effective.
- 3. Cyclosporine (if... not effective).

Brachio Radial pruritus

(Solar pruritus) (Fig 5/8)

(Nerve Trauma +
UVL → Mid outer arm.)

- Condition in w. there is:
 - ↳ itching
 - ↳ burning
 - ↳ Change in sensation
 - ↳ Lichenification, Hyperpigment., of Mid-arm.
 - ↳ Bruises.
- affect one or both arms sp. The outer aspect of Mid-arm.

Nerve damage.

- AET: d.t Cervical spine dis. that's show ↑↑
 & sunlight Exposure. (
 - ↳ Light: Eliciting factor
 - ↳ Spine dis: predisposing factor

- III.
 - Neurological assessment for Cervical Rib or In osteoarthritis
 - Sunscreen.
 - Capsaicin, local Anaesthetic
 - Amitriptyline. (ترىبتونول)

Hydroa Vacciniform

(updated ONNZ & Emol 2014)

(Vesicle)

(Vaccinia like scar)

Def. Rare photosensitive dermatosis ch-BY by (UVA)
Recurrent attack of: (after 6 hrs)

1. Hydroa: Fluid filled blister. (Maculopapular → Hgic blisters) ^{painful pruritic.}

2. Vacciniform scar: small pox like scar.

Age. 2 → Childhood 2 peak → 1-7 yrs
♀ > ♂ → Adulthood (rare) → 12-16 yrs.

Resolve at 20 yrs

Some cases ass. EBV ch-BY:
(H. Vacciniform like lesions)

- ① Severe wide spread (sunprotected)
- ② Systemic S & S (fever, HSM, EBV by PCR)
- ③ ↑ Incid of leuk. or lymphoma ✓

لوحيين قنطرة
تلك

- child (3-15), ♀
- Blister erupt
- Vacciniform scar
- DD
- ? Lymphoma

قنطرة
2015

Path.
F. 4: epid
cyt. degen.
immune. inflt,
thrombosis
Necrosis
? Both.

DD

Erythropoietic protoporphyria (EPP)

- disturbed porphyrin level.
- Burning in mins. of exposure.
- Wax like scarring (Not Varioliform).

th. 1. Photo-protection

2. Anti malarial
3. Antioxidants
4. phototherapy (desensitize)

5. H of EBV

6. Stem cell Transplant (if lymphoma)

NB

Hydroa Aestivalis

→ Mallorca Acne

also is childhood Vesiculo-papular photoeruption of unknown Aet. but differ from H. Vacciniform. in: "No Scarring"

Chronic Actinic Dermatitis: (UVB)

def. photosensitive disorder that represent the end stage of progressive photo sensitivity.

old names: . persistent light Reactivity.

. Actinic Reticuloid (Resemble: Reticulosis or Cut Lymphoma on Biopsy).

clinically - usually Elderly > 50ys. = occupational sun-exposure (farmers).

- Early → Lichenoid Late → Pseudolymphomatous (So called Reticuloid)

Early - Severely itchy & Excoriated papules & plaques later → Pseudo lymphomatous papules & plaques

- there may be:

- Nodules → Leonine face (= deep furrows)
- Generalized affection → Erythroderma & Generalized L.N.
- dyspig. (Vitiligo like).
- diffuse alopecia d.t severe prolonged rubbing
- Severe Itching → (± suicide)

Aet. unknown but ± Preceded by Eczema:-

- AD
- ACD
- Photocontact Dermatitis → UVB mainly.

Courses (life long) but some cases may show Spont. Resolut.

. 10% → 5%
. 20% → 10%

→ Allergens as (Compositae Plants, Rubber, Fragrances)

CAD

فقدان

[1] UVB

[2] HP:

MF

Band-like infiltrate of Histocytes & Lymphocytes... ± invade epidermis.
"Pautrier Microabscess"

Cells

Nuclear-like MF cells
Mitotic figure.

[3] CAD like CTCL

HP

Immunohisto. TCR

will differentiate

Q

.. DD Leonine Face:

- (- Leprosy
- (- Leishmania
- (- Lymphoma (T & B Cell)
- (- Leukemia
- (- Mastocytosis (Nodular)
- (- Sarcoidosis
- (- Amyloidosis (systemic)
- (- Proteinosis
- (- Histiocytosis
- (- Scleromyxedema (Mucinosis)

chemical & Drug-Induced Photosensitivity

Def: development of cutaneous disease as a result of the combined effects of a chemical and light. Exposure to either the chemical or the light alone is not sufficient to induce the disease; however, when photoactivation of the chemical occurs, one or more cutaneous manifestations may arise.

Types

[A] Phototoxic: Subtypes

- Phytophotodermatitis
- Pseudo-PCT
- Lichenoid DE

- SCL E

- Photo-onycholysis

- Slate-gray pigm.

[B] Photoallergic:-

Aetiology: Photosensitivity reactions may result from topical or systemic medications + exposure to the UV-A₁ (320-400 nm) (also visible light may induce). Most phototoxic reactions result from the systemic administration of drugs while Photoallergic reactions can be caused by either topical or systemic administration of the chemical. There are some Compounds that commonly cause both reactions.

it is often difficult to differentiate phototoxic from photoallergic reactions. However, they have a number of distinguishing characteristics (see Table below).

Feature	Phototoxic Reaction	Photoallergic Reaction
Incidence	High	Low
Amount of agent required for photosensitivity (Alergen)	Large	Small
Type of agent (Drugs)	usually systemic > Topical	Topical > systemic
Frequency of exposures	One	More than one
Onset of reaction after exposure to agent and light	Minutes to hours	24-72 hours (1-3 ds)
Distribution	Sun-exposed skin only	Sun-exposed skin, may spread to unexposed areas (face, dorsal hands, V area of chest)
- Clinical characteristics	Burning or stinging	ECZema like
- Hyperpigmentation	sun burn like + post inflamm. Hyperpigm.	(NO PIH) (itchy)
Mechanism	direct damage to tissue caused by a photoactivated compound (except PUVA)	Type IV hypersensitivity

Previous Sensitized

V area of chest

Spare

- Postauricular
- Submental
- upper eyelid

NB: Other less common skin manifestations of phototoxicity include pigmentary changes. A blue-gray pigmentation (With or without past history of burn like eruption) is associated with several agents, including

incid. Mechan. Agent

Type
amount
frequency
of exposure

onset
lesion
site
post

• Example of Photosensitizers:

- Tetracyclines
- Quinolones
- Naproxene
- Isotretinoin
- Antimalarial
- Dapsone
- Thiazides

•• Topical

- ← Sunscreens
- ← SFU
- ← Coal Tar.

Investigations: (قراءة عناوين)

1. Assess urine porphyrin levels (to diff. between pseudo-porphyrin and porphyria cutanea tarda), ANA and anti-Ro (SS-A)

2. Photopatch testing is an important tool in the diagnosis of photoallergic contact dermatitis.

↳ drug + Sun exposure of skin

3. Histologic Findings

• In acute phototoxic reactions

[. Spongiosis

[. KC Necrosis (sun burn cells)

[. Mixed dermal Infil.

[. if pigm. is present its either dit

↳ Melanophages

or
↳ deposit of metabolites in dermis

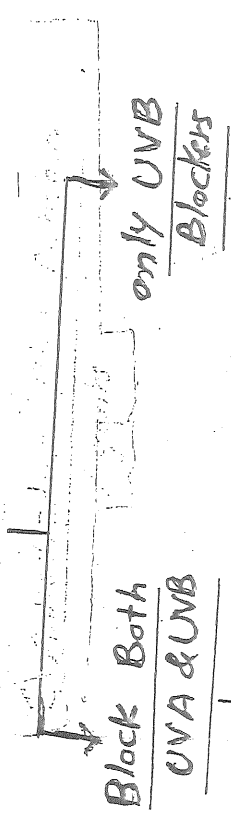
• Photoallergic reactions : as ACD (spongiosis + mixed dermal Infil.) but presence of KC Necrosis suggest Photoallergy.

Treatment

- 1- The main goal of treatment is to identify the photosensitising agent and if possible to avoid it. In cases where medication is being taken to treat an existing condition and can not be discontinued, patients should be advised to follow sun protection strategies, including wearing sun protective clothing and using sunscreen.
- 2- Topical corticosteroids

photo test → light + skin

Systemic



Antimalarials

Anti oxidants (± used < Systemic)

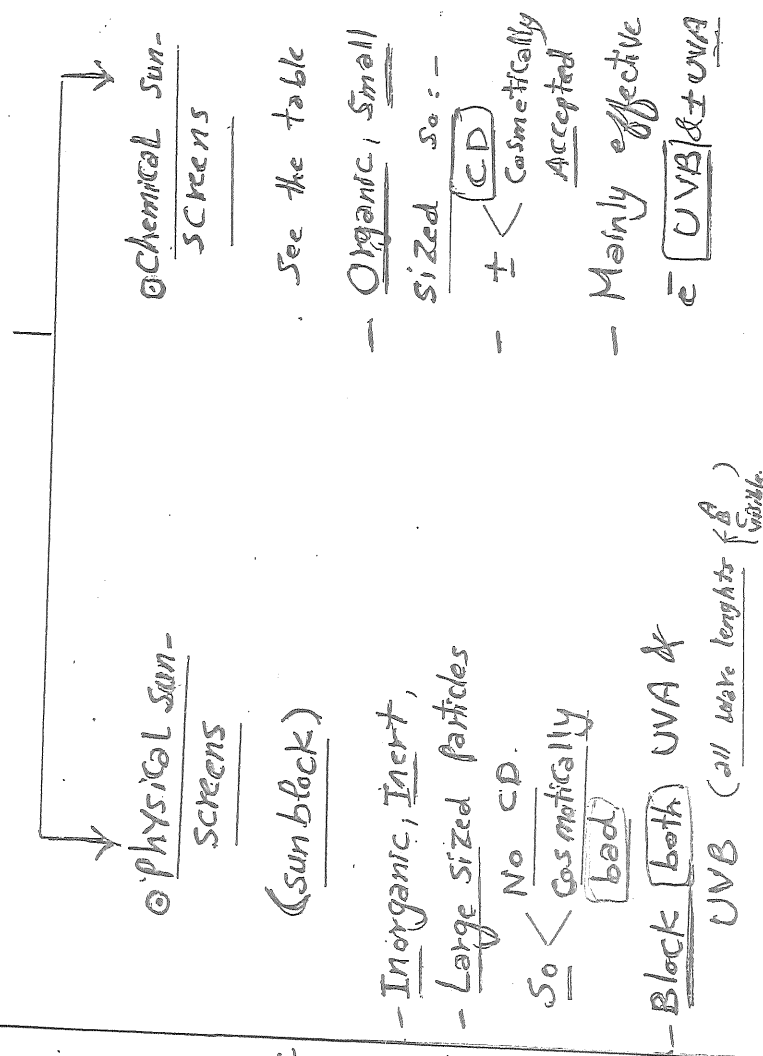
- Vit. C (1g/ml)
- Vit. E (400 IU/d)
- Carotenoids eg β Carotene (Adult: 60-180 mg/d, child: 30-90 mg/d given to maintain level 600 mg/d)
- Green tea
- Poly podium Leucotomas
- others: NSAIDS, selenium.

علامة لونه في أي مرقع متعلق بالشمس ألبت Anti oxidant

Mechanism of photoprotective action of Antioxidants

- ① Scavenging free radicals & ROS
- ② ↓ No of UV induced sunburn cells
- ③ Preserving L.Cs.

Topical



(Sun block)

Inorganic, Inert, Large sized particles, No CD, So < Cosmetically bad

Block both UVA & UVB (all wave lengths)

Mechanism: Light Reflexion & Scattering

as: Zinc oxide, Titanium dioxide, Kaoline

Al cream, Zinc oxide, Ultracare cr.

Mechanism:

Light absorption → harmful Energy is converted to non harmful one.

Chemical absorbers

The table below is a list of some of the common chemical absorbers available and the protection they provide against the UV range.

Chemical	UVB (290-320nm)	UVA II (320-340nm)	UVA I (340-400nm)	→ <i>مقاومة</i>
Aminobenzoic acid derivatives				
✓ PABA	Partial	None	None	
Glyceryl PABA	Partial	None	None	
Padimate O	Partial	None	None	
Roxadimate	Complete	Partial	None	
Benzophenones (الأقوي والأفضل) ✓				
✓ Dioxybenzone	Complete	Complete	Partial	
✓ Oxybenzone	Complete	Complete	Partial	
Sulisonbenzone	Complete	Complete	Partial	
→ <u>AVO benzone</u>				
-Cinnamates (easily removed ← <i>ست. كم. يسهل إزالته</i>)				
✓ Octocrylene	Complete	Complete	Partial	
Octyl methoxycinnamate	Complete	None	None	
Salicylates				
✓ Homosalate	Partial	None	None	
Ethylhexyl salicylate	Complete	None	None	
Trolamine salicylate	Complete	None	None	

* Chemical absorbing sunscreens often contain a combination of ingredients to get coverage against both UVB and UVA radiation. Some are also combined with physical blockers.

* PABA should be avoided in children younger than 6 months because it can cause skin irritation.

* Efficient (Benzophenones, Octocrylene), less efficient (PABA and Salicylates).

other groups

- ✓ Akobenzone } NO UVB, Block of UVA < I
- ✓ Ecamsule }
- Bimatrimol (Tinosorb) all

NB. Most sunscreens contain both physical & chemical preparations.

HL

Polypodium Leucotomos

- plant extract that has antioxidant effect & DNA protective effects
- used in combination with green tea extract & beta-carotene in New Zealand under the name of HelioCare

• Some definitions of sunscreens:

①. SPF: $\frac{\text{MEDs Protected by } 2\text{mg/cm}^2 \text{ of sunscreen}}{\text{MEDs unprotected}}$

What does it mean that: SPF 15; this means that this sunscreen provides 15 times protection (from UV) when applied than when not applied or if \bar{e} unprotected; MEDs occur after 10 minutes — this sunscreen prevent MED for upto 150 mins.

$$\left(\frac{150}{10} = 15 \right)$$

• The higher the SPF the better of skin protection.

• SPF of $\begin{matrix} 10 & \xrightarrow{\text{protect}} & 90\% \\ 15 & \longrightarrow & 93\% \\ 30 & \longrightarrow & 97\% \end{matrix}$ } also compensate for underapplication.

30+ كبر السن
(Above 50+)

• SPF > 30; Expressed as SPF 30+

• SPF = sun protection factor $\xrightarrow{\text{FDA 2007 change Name}}$ Sunburn Protection Factor

②. Sunscreen substantivity: the ability of the product to maintain its efficacy under the stress of prolonged exercise, sweating & swimming; what ever Repeat application several times \rightarrow during exposures \rightarrow After swimming & sweating.

③. Water Resistant : SPF maintained for 40 mins after Immersion.

④. Water proof : SPF maintained for 80 mins after Immersion.

FOA 2007
✓
Very Water Resistant

Whatever, some authors don't agree with those Resistant & proof & recommended application After swimming & sweating.

NB : Most sunscreens (chemicals) effective in shorter wave lengths (290-320) but Benzo phenones provide more UVA protection. (against UVAI).

⑥ Physical sunscreen may absorb some UVL \rightarrow Free Radicals so some products contain Silicon Coat for Absorption of these free Radicals.

UVAI & UVAII

* Sun protection doesn't Means use of sunscreen

only but equals = Sun Protection Program

للرشفة
نيرة

1- Avoid mid-day sun (10 am - 4 pm)

2- Seek shade.

3- Wear protective clothes/hats, sunglasses

أو عيشة

4- Use sunscreens (Topical \leftarrow physical \leftarrow chemical \leftarrow systemic) Antioxidant

Def. clothing that made of UV protective fabrics

protective fabrics : these are fabrics that achieve a minimum UV protection Factor (UPF \rightarrow SPF)

& at least UPF 15 after the equivalent of 2x of NL wear & tear.

UV Protective clothes ch-BY

- 1- 100% Polyester (contain benzene ring that absorb UVL)
2. dark clothing (dye absorb UVB 5 times > white)
3. Tight ly Woven fabrics
- 4- Long - sleeves
 pants
 skirts & shirts
 Collars & high Neck lines.
- 5- Loose clothing. (Folds of loose clothing → double fabrics sun protection).
6. Coverup with dry clothes after swimming or getting wet.
7. Wash & detergent that contain optical Fluorescent brightness. (act like dyes absorb UVL).
8. Hats with (4 inch) brim all around.
9. sunglasses Blocking UVA & UVB

UV Index

- 1- بلايش فروج صم (٢٤-١)
- 2- ماشي ز الفضل
- 3- الملابس
 بولستر
 غامقة
 طرية
 موية
- 4- نظارة شمس
- 5- برنطة
- 6- شمسة
- 7- Rapid sunscreen + Antioxidant

→ For Any Patient & photosensitivity

How to use sunscreens ?

To get the best protection from your sunscreen you should consider the following points:

- Use a good broad-spectrum sunscreen of at least SPF 15 and made up of a benzophenone chemical absorber plus a physical blocker (titanium dioxide or zinc oxide).
- Apply sunscreen liberally to all sun-exposed areas so that it forms a film when initially applied. Most people use sunscreens improperly by not applying enough.
- Dual application technique : It takes 30 minutes for sunscreen to be absorbed by the skin and it can be rubbed off very easily, so apply it at least half an hour before going out in the sun. Reapply after half an hour after exposure (imagine you are painting a wall - two coats of paint provide a more even cover than one). This dual application technique is designed because the most common cause of sunscreen failure is under application (many studies showed that most users apply 25% -75% of standard amount , so SPF is much reduced).

قبل الخروج بنصف ساعة
وبعد " " " "

(To avoid skip areas)

NB: The standard amount is that: one teaspoon should cover the face, each arm, each leg and exposed parts of neck and shoulders. Two teaspoons can cover the entire torso.

ملعقة صغيرة لكل منطقة

- Re-apply sunscreen every 2 hours if staying out in the sun .
- Re-apply immediately after swimming, excessive sweating, or if rubbed off by clothing or towelling. This should be the case even if the product claims to be "water resistant" (Activities such as sweating and swimming degrade its effectiveness. The FDA is banning what it calls misleading labeling on sunscreens such as the use of the words sunblock, waterproof, and all day protection will no longer be used)
- Insect repellents reduce the sunscreen's SPF so when using together, use a sunscreen with a higher SPF and re-apply more often.
- Which sunscreen, if any, should I use?

كلام غير صحيح

*Alcohol-based lotions, sprays or gels are better for oily or hairy skin, Creams are suitable for dry skin, and milky lotions are the easiest to apply. Special sticks are suitable for noses, lips and around the eyes.

18 23

What about Vitamin D?

If you have fair skin you may need only 5 minutes of midday summer sun activity in shorts and t-shirt without sunscreen to make enough. You will need longer or greater skin exposure if your skin is darker. Being physically active outdoors helps you make more Vitamin D than resting in the sun. If you are over 50 years old (ageing skin is not as good at making Vitamin D), immunosuppressed or have had previous skin cancers, you are better to apply sunscreen and talk to your doctor about Vitamin D supplements.

Sunscreen applied to babies (below 6 months) on limited areas. Vitamine D supplementation may be recommended with the most stringent sunprotection practices (some authors didn't recommend sunscreen for children beow 9 months but other sun protection programs should be carried out).

- Male sexual dysf. ??

سوال امتحان

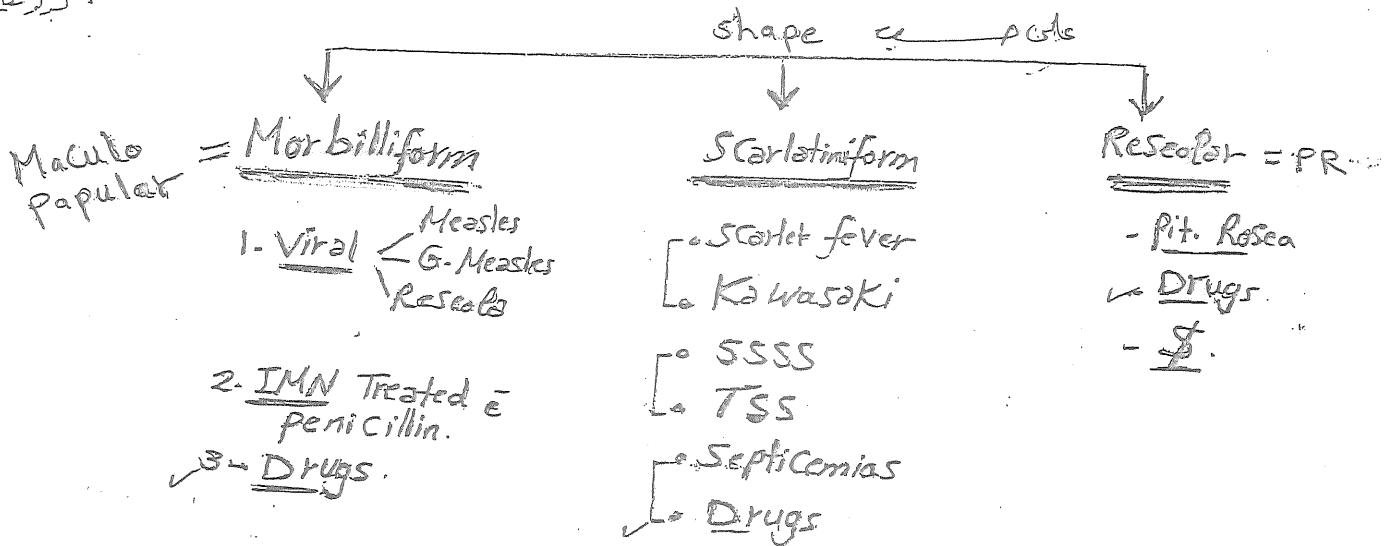
Erythemas

• Erythema
• Erythema
• Erythema
• Erythema
• Erythema
• Erythema
• Erythema
• Erythema

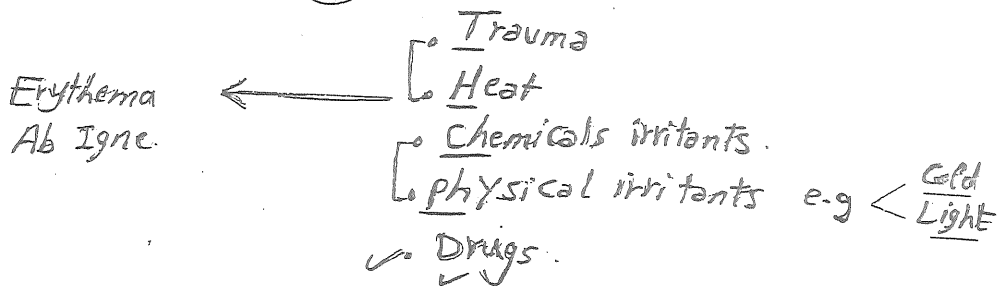
def. change in color of skin d.t dilatation of Bvs specially Those of papillary & reticular dermis. As arteries & Veins may be involved; the color can vary from pink to dark red to Violaceous ^{artery} _{venous}

لثنية
م/د/م
ب/لثنية

Types: A- Diffuse:



B- Localized:



C- Palmar Erythema:

- pregnancy
- Thyrotoxicosis
- SLE
- RA
- LCF ← liver cell failure
- Familial
- Computer

Computer induced skin disease?

سوال (سجّان)

D

Annular (Figurate)

Gyrate

Erythemas: see below

E

Other Types:

سجّان

1. Flagellate Erythema: (Linear streaks)

- Chemotherapy \rightarrow Bleomycin, docetaxel
- Dermatomyositis
- Adult onset Still's dis.
- Shiitake Mushroom dermatitis

2. Reticulated: Cut. PAN. & EAI

Erythema ab igne

3. Intermittent: Flushing

سوال
سجّان

NB: Most Erythemas last for days \rightarrow Months
but some last only for minutes (Flushing).

By fire → SCC

Erythema ab igne (EAI)
(Toasted skin syndrome, Fire stains) (Laptop thigh / hot Water Bottle rash).

Def: localized areas of reticulated erythema and hyperpigmentation due to chronic and repeated exposure to infrared radiation heat at a lower level than that which causes a thermal burn.

(IR)

Pathophysiology: repeated heat exposure in the range of 43-47°C that induces injury to the epidermis and superficial vascular plexus. Histopathologic changes similar to those seen in solar-damaged skin.

- Although the pathogenic mechanisms in erythema ab igne are poorly understood, one study has shown that moderate heat acts synergistically with ultraviolet radiation to denature DNA in squamous cells in vitro.

(Heat + UV)
→ DNA denaturation
↓
SCC

The following is a summary of heat sources reported to cause EAI: Heating pads, Hot water bottles (For pain relief in cancer pancreas and myositis), Electric stoves/heater, Open fires, Coal stoves, Peat fires, Wood stoves, Steam radiators, Car heaters, Heated reclining chairs, Heating or electric blanket, Hot bricks, Infrared lamps, Microwave popcorn, Laptop computer, Automobile seat heater, Hot bathing

Epidemiology more in middle aged obese women.

C/P: Transient, blanchable reticulated erythema → persistent erythema → reticulated hyperpigmentation → development of: (AK) (SCC) (Merkel) cell carcinoma

- Typically, erythema ab igne affects the legs of women aged 40-70 years who use indoor fire as a heat source. Erythema ab igne reportedly affects the face and/or palms of cooks who work over an open fire. EAI of the abdomen, flank or mid-back may reflect an attempt to relieve pain from inflammation (e.g. pancreatitis, peptic ulcer disease) or malignancy (e.g. pancreatic, gastric). Other sites are according to heat exposure

- Other clinical variants of erythema ab igne are as follows:

- 1 - **Bullous EAI** (associated with normochromic normocytic anemia and subclinical hypothyroidism)
- 2 - **Hypertrophic or hyperkeratotic and Keloidal EAI** (associated with lymphedema)
- 3 - **Poikilodermatous EAI**

Pathology (A) epidermal and dermal atrophy, abnormal elastic fibers, capillary vasodilation and dermal pigmentation (both melanin and hemosiderin). Focal (E) hyperkeratosis and dyskeratosis are noted along with squamous atypia. (F) → SCC

→ 157

Differential diagnosis: EAI needs to be distinguished from livedo reticularis, which is a temperature-sensitive vasculopathy that favors the extremities but only occasionally develops associated hyperpigmentation. The presence of telangiectasias along with atrophy and hyperpigmentation raises the possibility of poikiloderma and its various causes. MF, dermatomyositis.

DX → livedo reticularis
→ Poikiloderma
→ MF
→ DM

Figurate (annular, gyrate) Erythemas

Figurate erythemas are characterized by lesions that are annular, arciform or polycyclic in configuration. Although a wide range of cutaneous diseases can have an annular appearance, there are four 'classic' figurate erythemas:

- 1-Erythema annulare centrifugum
- 2-Erythema marginatum
- 3-Erythema gyratum repens
- 4-Erythema migrans
- 5-Annular erythema of infancy
- 6- Annular erythema associated with extractable nuclear antigens

بولونيا ذكر اول ؛ لكن Rook اضاف النوعين هـ و آ.

Erythema Annulare Centrifugum (EAC)

Etiology & Pathophysiology:

EAC usually Idiopathic but it may be due to Hypersensitivity reaction to variety of Agents including:

1- Infection:

- Bact. → E. coli & strept.
- viral → EBV, Molluscum, HZ & HIV
- Fungal → Dermatophytes & Yeast (sp. Candida).
- Parasitic → ascaris & scabies.

Wolff's Isotopic phenomena.

2- Drugs: specially

- NSAIDs ✓
- Gold
- diuretics ✓
- Antimalarial ✓
- piroxicam
- penicillin ✓
- Aldactone.

3. M.G:

- Leukemia
- Lymphoma
- Cut. Tms (SCC)

4 others:

- Food (Tomatoes)
- stress, Menses, pregnancy
- Sarcoidosis, SS, CA

Epidemiology - Age → any, but peak usually at 50 yrs.

Sex → No predilection

Race → No predilection

NB AD inheritance reported « Familial EAC »

IP The lesions start as Erythematous papules that spread Peripherally while clearing Centrally & Enlarges at a rate of 2-5 mm/d → Annular, Arciform, Figurate or Poly-cyclic (Festooned) plaques or patches.

دایره
بتوسع

There are 2 clinical varieties:

A Superficial Type :-

- Scaly → desquamation at inner margin « Trailing scales ».
- Pruritic
- non indurated or infiltrated.

Erythema Annulare Centrifugum (EAC)

• Etiology & Pathophysiology:

EAC usually Idiopathic but it may be due to Hypersensitivity reaction to variety of Agents including:

1- Infection:

- Bact. → E. coli & strept.
- Viral → EBV, Molluscum, HZ & HIV
- Fungal → Dermatophytes & yeast (sp. candida).
- Parasitic → ascaris & scabies pubis.

"Woolf's Isotopic phenomena"

2. Drugs: specially

- NSAIDS ✓
- Gold
- diuretics ✓
- Antimalarial ✓
- piroxicam
- penicillin ✓
- Aldactone.

3. MG:

- Leukemia
- Lymphoma
- Cut. Tms (SCC)

4 others:

- Food (Tomatoes)
- stress, Menses, pregnancy
- Sarcoidosis, SS, CA

• Epidemiology: Age: → any, but peak usually at 50 yrs.

Sex: → No predilection

Race: → No predilection

NB AD inheritance reported « Familial EAC »

IP The lesions start as Erythematous papules that spread Peripherally while clearing Centrally & Enlarges at a rate of 2-5 mm/d → Annular, Arciform, Figurate or Poly-cyclic (festeoned) plaques or patches.

دايره
بتوسع

There are 2 clinical varieties:

A Superficial Type:-

- Scaly: → desquamate at inner margin « Trailing scales ».
- Pruritic
- non indurated or infiltrated.

[B] deep Type EAC:

- < Non scaly
- < Non pruritic
- Indurated → = deep

المقن
الشمي

distribution of lesion: usually thighs & legs but may affect UL, Trunk & Face with sparing xx of palms & soles.

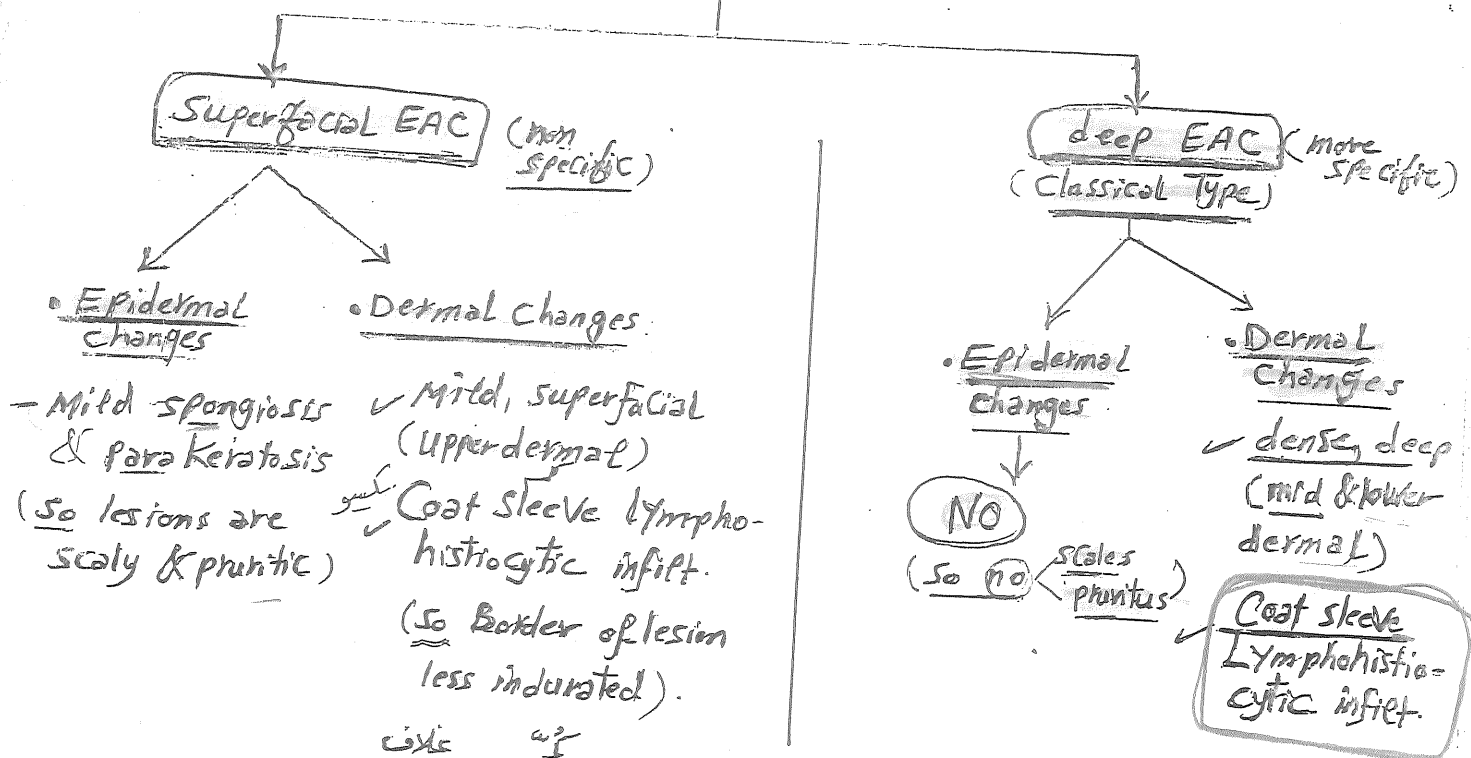
Course: → Ws-ms

Exacerbation & remission may occur (with flake or recurrence of Et.)

→ No residual scarring (but ±):
Post-hyperpig. "or" purpura.

⇒ NB White banding of Toenails reported in 25% with EAC.

• Histopathology



أهم حاجة
البارالمعي

علاف
Coat Sleeve
infiltr.

= infilt. is tightly Cuffed around the BVs.

Treatment (Non Specific):

- ① # of underlying possible Etiology e.g. Dermato-phytosis.
- ② Symptomatic # e.g. Antihistamines.
- ③ Topical Cs to the active border (beneficial)
- ④ Some authors → Empirical antibiotics & antifungal (Itracon or Terbinafin) → Cipro or Azithro.
- ⑤ Systemic Cs → remission may occur but recurrence is common.
- ⑥ Case reports:

Exhausted
Workup for Mg
Not indicated as
the reln bet
EAC & it is not
consistent

مفروضه علاقه كابت
Mg ع

- Metonidazole ✓
- Calcineurine inhibitors (CIs)
- Calcipotriol
- IFN- α → Dramatic in infantile EAC
- Etoncept
- intraarticular Hyaluronic acid.
- EAC + Hyper Eosinophilic synd → Dapsone
Keto Conazole
Septin.

HL

Wolf's isotopic response

The term isotopic response refers to the occurrence of a new skin disorder at the site of another, unrelated, and already healed skin disease.[2] It was first defined by Wolf et al in 1985 and hence is also known as Wolf's isotopic response.[3],[4] The term "isoloci response" has also been suggested. The isomorphic response, first defined by Koebner, indicates the appearance of typical skin lesions of an existing dermatosis at sites of injuries.[2]

The differences and similarities between these two terms are obvious.[1],[2],[5] The isomorphic response describes the appearance of a skin lesion which is morphologically similar to an existing skin disease at the site of an injury of any kind. Thus the term "isomorphic" means "the same morphology" (as the existing disease). The term "isotopic response", on the other hand, describes the occurrence of a new, unrelated disease that appears at the same location as a previously already healed disease; hence "isotopic" means "at the same place".

= Koebner

نفس المرض
في نفس المكان
الجمع

(مرض جديد مكان مرض قديم ملتئم)

The localization of skin diseases remains one of the most elusive problems in dermatology.[2] The proposed etiologies of isotopic response are viral, immunologic, neural, vascular and locus minoris resistentiae (a site of lessened resistance). Most cases of isotopic response have been described in healed lesions (scars) of herpes zoster. The second disease has been reported to be granuloma annulare, Kaposi's sarcoma, leukemia cutis, metastasis, sarcoidosis, acne, lichen planus, granulomatous folliculitis, tinea, verrucae plana, molluscum contagiosum, squamous cell carcinoma, basal cell carcinoma, or multiple epidermoid cysts.[2],[3],[6],[7],[8],[9] A recent report describes herpes simplex appearing on a scrofuloderma scar.[4]

Ref.1- Lee HW, Lee DK, Rhee DY, Chang SE, Choi JH, Moon KC, et al. Erythema annulare centrifugum following herpes zoster infection: Wolf's isotopic response?. Br J Dermatol. Dec 2005;153(6):1241-3
2-Sharma RC, Sharma NL, Mahajan V, Sharma AK. Wolf's isotopic response: Herpes simplex appearing on scrofuloderma scar. Int J Dermatol 2003;42:664-6.

ERYTHEMA GYRATUM REPENS (Gammel's disease)

EGR

شبه
دوائر الخشب
و تتحرك

٥٧٧٥٧

Key features

- A figurate erythema that is migratory and composed of concentric rings with a wood-grain appearance
- It represents a paraneoplastic phenomenon and the most common underlying neoplasm is carcinoma of the lung
- The lesions may have associated pruritus and scale, and they characteristically exhibit rapid migration (up to 1 cm per day)
- The cutaneous lesions resolve when the neoplasm is successfully treated

def. Type of Figurate Erythema ch BY: cutaneous
[Migratory Wood-grain like
Ass. underlying Cancer Lung.

HL Et. & Pathophysiology:

- ① Cross Antigenicity bet $\left\{ \begin{array}{l} \text{skin} \\ \text{TM} \end{array} \right.$
- ② TM \rightarrow Alter cut. Ag \rightarrow reacts
- ③ TM Ags + Ab \rightarrow deposit in skin

EGR like lesions \pm Seen in:
BP, EBA, LAD, Annular,
T. Imbricula, PRP
HP \rightarrow Non specific.

Epidemiology: Age \rightarrow Adults > 40 (but $\pm 16-75$; mean 63)
Sex \rightarrow M:F = 2:1

CIP:

EGR is para Mg

cut. lesions

Multiple annular Erythematous lesions with chic Wood-grain or Zebra like appearance
(Rings within rings) on $\left\{ \begin{array}{l} \text{Trunk \&} \\ \text{Extremities} \end{array} \right.$
The edge covered with scale &
show Rapid migration $>$ EAC
(upto 1cm/d)
May be pruritic

Associations.

- 1- Cancer: (85%) usually
Lung \rightarrow $\left\{ \begin{array}{l} \text{Breast} \\ \text{Stomach} \end{array} \right.$
- 2- Other cut. lesion: -
- Acq. Ichthyosis
- PPK
- Hypereosinophilia.

Course: \rightarrow NB. lesions usually

ERYTHEMA MARGINATUM
RHEUMATICUM

EMR

Rh Fever
child

Key features

- Migratory annular and polycyclic erythematous eruption
- Cutaneous manifestation of acute rheumatic fever
- Associated findings include carditis, migratory polyarthritis, Sydenham's chorea and subcutaneous nodules
- Seen more commonly in children than in adults

def. Type of figurate Erythema occurs in the setting of active Rheumatic fever.

Etiology & Pathophysiology:

• Rheumatic fever is an abnormal Immunological response To a preceding infection & group A Beta hemolytic streptococci & clinically by Triad of: GABHS

(FAC)

- Fever
- arthritis
- Carditis

→ affect 3% of untreated pts. (5-15%)

• <10% of R. fever show ESR

CIP : Arciform, Annular or Polycyclic Ch By:

- ① Affect Trunk, Axillae & proximal Extrem.
- ① Migratⁿ rate \approx 4-24 cm/d
- ① Exacerbatiⁿ & remission over (hrs-ds).

- No specific HP.
- No \uparrow TTT (Self limiting & TTT of R. Fever has No effect on EMR)

NB: other cut. Manifests of R. fever:

- SC Nodules (Similar to Rh Nodules)
- urticarial like lesions.

ERYTHEMA MIGRANS (Lyme disease, Lyme borreliosis, Afzelii's disease)

Key features

- Annular erythema develops at the site of the bite of a *Borrelia*-infected tick.
- Several species of *Ixodes* ticks are infected with different genospecies of *Borrelia burgdorferi*.
- Erythema migrans represents the initial cutaneous manifestation of disease and is seen in 60-90% of patients diagnosed with the disease.
- Multiple secondary lesions that are smaller in size can occur as a result of spirochetemia or lymphatic spread.

Lyme disease

def. Multisystem infect- first presented with cut. findings
Caused by Gram -ve Spirochaeter Genus *Borrelia* & Transmitted by hard ticks genus *Ixodes*.

Etiology: Spirochaetes of genus *Borrelia*: (HL)

• There are 11 species.

• 3 of them causing Lyme dis. & collectively named *Borrelia Burgdorferi sensu lato* Complex:

subspecies	<i>B burgdorferi sensu lato</i> subspecies (HL)	
<i>B burgdorferi sensu stricto</i>	Geographic distribution	Associated disease
<i>B garinii</i> ,	all North American and Europe	Classical lyme (But no Lymphocytoma)
	exclusively in Europe	-Neuroborreliosis
<i>B afzelii</i>	Europe	-Lymphocytoma cutis
		-Acrodermatitis chronica atrophicans (most common organism)
		-Lymphocytoma cutis
		-/+ Morphea
		-/+ LSA - Anetoderma

Transmitted by the bite of Hard ticks species (HL)
Ixodes - subspecies

I. Scapularis → north eastern & midwestern US

I. pacificus → North western US

I. ricinus → Europe

I. ovatus → asia

• CIP (has 3 stages as follows)

• Age: Bimodal (children 5-14 & Adult: 30-50)

Stage	Manifestations
I-Early disease: 1-localized (to site of inoculation)	<ul style="list-style-type: none"> Erythema Migrans (1-2%) Regional lymphadenopathy LN Mild Constitutional manifest. (FAHM)
2-Disseminated (B.I. & Lymphatics)	<p>A-Cutaneous manifestations:</p> <ul style="list-style-type: none"> Disseminated Erythema Migrans Lymphocytoma (Europe) (1%) <p>B-Neurological:</p> <ul style="list-style-type: none"> Meningo-polyradiculoneuritis (Bann Warth Synd.) Cranial neuritis Bell's palsy <p>C-Musculoskeletal:</p> <ul style="list-style-type: none"> Arthralgias, Arthritis Myositis <p>D-Cardiac:</p> <ul style="list-style-type: none"> Pancarditis Myopericarditis Tachycardia Atrioventricular block <p>C-Lymphatic:</p> <ul style="list-style-type: none"> Regional or generalized lymphadenopathy <p>D-Others:</p> <ul style="list-style-type: none"> conjunctivitis and iritis hepatitis non productive cough microscopic hematuria or proteinuria
II-Late(chronic)disease:	<p>A) Cutaneous manifestations:</p> <ul style="list-style-type: none"> Acrodermatitis chronica atrophicans <p>B) Neurological:</p> <ul style="list-style-type: none"> Encephalopathy Encephalomyelitis Neuropathy <p>C) Musculoskeletal:</p> <ul style="list-style-type: none"> Chronic arthritis

1- Erythema Migrans (ليثا مريمن)

(Erythema Chronicum Migrans)

incid: 60-90% of cases of Lyme dis.

onset (Ip): 1-2 wks.

durat: (if untreated): < 6 wks.

CIP: The classical lesion starts as an ^{asymptomatic} Erythematous macule or papule that expands peripherally over days-ws with diameter usually > 5 cm (CDC criteria) or average 16 cm (but ± upto 70 cm). often Central Punctum may be seen (bite); Lesion ch.BY:

Center of lesion in:

North America: darker or of same color of periphery (Homogenous uniform lesion)
Santor darker

2 Periphery; raised, nonscaly, bluish red & warm

15

ECM may be ass. with:-

Site:

Regional
L-N

(FAHM)
Mild Constitutional
Manifests.

SOME NBS (Ened. 2009)

In 25% of cases
Multiple ECM lesions appear
at either Multiple bites
or disseminated

disseminated ECM
differs from Lyme in:-

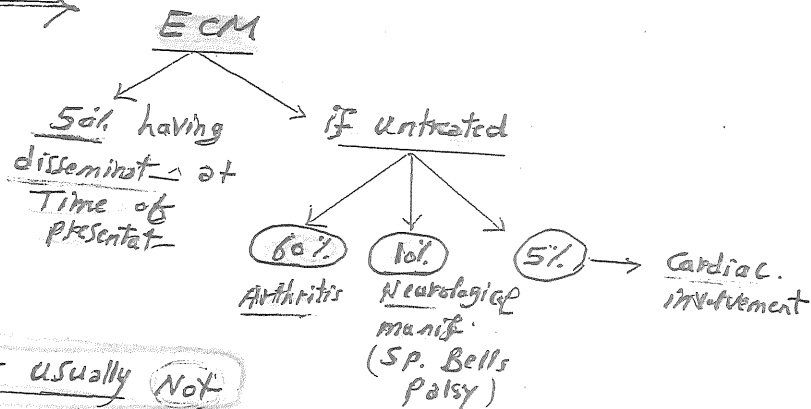
- [Multiple]
- [Smaller]
- [less pronounced]
- [appears ds. 4w from onset of 1st ECM...]

① Classic target lesion with concentric rings of erythema, which often show central clearing (annular configuration). Although this morphology was emphasized in earlier North American literature, it only represents approximately 40% of erythema migrans lesions in the United States. This pattern is more common in Europe. & because it has more chr. course → ECM (chronicum).

② Location: Location of the bite is an important diagnostic clue. Ticks tend to feed in areas in which natural barriers prevent their forward progress, such as the popliteal fossa, groin, and axilla, or in areas in which elastic clothing or bra straps impede their journey. The thorax and trunk also are common spots. In children the hairline and scalp are especially common locations.

③ Rashes very similar to erythema migrans have been reported in the southern United States from which *B. burgdorferi* cannot be cultured. This disease is called southern tick-associated rash illness (STARI), or 'Master disease'. As a group, distinctions can be made between classic erythema migrans and this illness, but significant overlaps exist such that the differences are not useful in diagnosing individual patients.

④ →



⑤ High fever usually Not

present in ECM & if it is present → Suspect

A- Alternative diagnosis

B- Additional tick born inf:

- Babesiosis
- Ehrlichiosis
- Anaplasmosis.

Even though the lesion expands centrifugally, *B. burgdorferi* organisms have been found both in the center and the periphery of lesions of erythema migrans. The persistence of the spirochete in the skin for a long time after the tick bite may be due to an absence of the production of interferon-γ and an ineffective immune response^[20]. Also, different immune responses to the various genospecies of the *B. burgdorferi* sensu lato complex (*B. burgdorferi* sensu stricto, *B. afzelii*, *B. garinii*) may lead to different clinical presentations^[22] (e.g. borreliac lymphocytoma in Europe but not the US; see Ch. 74).

Histopathology

as Warthin-Starry stain (E.E.S)

1. Routine → Non specific similar to deep Gyrate Eryth. ± Eosinophils & plasma cells in infiltrate
2. Immunohistochem: - ↓ Les in dermis
- CD4, CD45 RO, Macrophages
3. silver stain → detect Borrelia.

Borrelia Lymphocytoma

(Lymphocytoma Cutis = Lymphadenosis Benigna Cutis)

Def, Histopath, Ht → See pseudolymphoma.

Same NBS: ① Caused by Borrelia afzelii & garinii (so occurs in Europe & Not in USA)

② Site: children → Ear lobe

• Adult → areola.

• less common on: Trunk, genitalia & extremities.

③ present in (~1%) of Lyme dis.

also
Borrelia Lymphomas
(are) identified

ACR
only dis.
that doesn't x
small spots.
solit

Acrodermatitis Chronica Atrophicans [ADCA] (Herkheimer disease)

def. Cut. manifestation of Late (Chronic) European Lyme dis.

Usually caused by B. Afzelii (ass: long standing persistence in skin).

Clp: - Usually occurs after (6 mos - 8 yrs) from onset of inf.

- More common in ♀ 40-70 yrs.

- It is a Biphasic disorder: 2 stages

(but ± occur at same time)
عند نفس الوقت مع برائته

Early inflammatory stage "unilat"

Insidious onset of ACAL
Erythematous-Violaceous
Nodules & plaques @ waxing & waning course for years.

Late atrophic stage

- Atrophy ± glistening "Cigg.
Paper appearance @ prominent
BVs.
- There may be: SC Nodules at forearm & legs

Thin
Atrophic
Translucent
Wrinkled
↓
Faint
Sweaty
papules

Diagnosis of Lyme dis

18

1st during different stages

A during ECM :-

① Clinical diagnosis: CDC accepted diagnosis for lesions $> 5\text{cm}$ but some cases show smaller lesions & so CDC defin. is for surveillance only (most cases have diameter $\approx 16\text{cm}$).

② Therapeutic diagnosis: by giving Doxy or Amoxy & observe for improvement.

③ Serological diagnosis:

- disadv. usually become +ve in 3-6 wks after inf. & the waiting for this period to confirm the diagnosis will \rightarrow dissemination.

- Methodology: CDC instruct 2 steps:

1st \rightarrow ELISA or IF.

2nd \rightarrow WB (for +ve or +/- ELISA or IF)
if detect IgM against 41KDa flagellar Ag.

2008. Newer assays detect of C6 peptide
 \downarrow
VSIE

④ Culture, HP & PCR ^{Non-specific}

B During L. Curtis, Biopsy + chc site

C Acrodermatitis chronica stage: Serology is +ve ✓

Treatment

- ①. Early localized \rightarrow 2-3 wks
 - ②. Mild Early dissim. or Mild late \rightarrow 2 wks - 4 wks
 - ③. Severe " " or severe " \rightarrow 2 - 4 wks
- Doxy 100 (1x2)/d
or
Amoxy 500 1x4
[ceftriaxone 2gm 1x1]

Annular erythema of infancy

def. EAC like lesions that may affect infants.
AET as EAC but:

1. Dermatophytosis & Mg → Not considered
2. Consider:
 - LE
 - Maternal Transplacental autoantibodies
 - Heavy intest. candidal colonization
 - EBV.
 - Pityrosporum inf.

CIP → EAC like

Path. → EAC like but \bar{e} prominent Eosinophilic infiltr. (Neutrophilic variant reported).

- HH →
1. HH of underlying inf.
 2. Na Cromoglycate
 3. IFN- α

Eosinophilic Annular Eryth
 variant of Wells

Annular erythema associated with extractable nuclear antigens

def. EAC like lesions affecting patients with ANAs usually young adults.

CIP EAC like but differs in:

- ① Photosensitive distribut- (Specially face)
- ② Edge more broad > EAC.

AET = SS with ANAs:

1. NLE cases \bar{e} Anti Ro & U.RNP
2. SS & SLE → cases \bar{e} anti La & U.RNA

Table 20.1 -- Differential diagnosis of figurate erythema.

DIFFERENTIAL DIAGNOSIS OF FIGURATE ERYTHEMA			
Disorders	Clinical features <i>C/P</i>	Histologic findings <i>H/P</i>	Cross references
1-Transient lesions (typically lasting <24 hours)			
<u>Urticaria</u>	Transient and recurrent wheals; pruritus	Superficial perivascular infiltrate of eosinophils and lymphocytes; occasional neutrophils	Ch. 19
<u>Erythema marginatum</u>	Polycyclic erythematous eruption; antecedent group A streptococcal infection; additional manifestations of acute rheumatic fever, e.g. arthritis and carditis	Scant perivascular infiltrate of neutrophils in the papillary dermis without vasculitis	See text
<u>Erythema marginatum-like lesions of hereditary angioedema</u>	Transient polycyclic erythematous eruption; favors trunk; precedes or accompanies episodes of angioedema	Minimal to no inflammatory infiltrate; dense perivascular and interstitial dermal deposits of bradykinin	Ch. 19
<u>African trypanosomiasis</u>	Annular erythematous patches on the trunk associated with fever spikes	Perivascular lymphocytic infiltrate; parasites are occasionally seen within the dermis	Ch. 82
<u>Erythrokeratoderma variabilis</u>	Transient gyrate or circinate erythematous patches (usually fade/migrate within a few hours); also fixed figurate hyperkeratotic plaques; <i>GJB4</i> mutations	Scant perivascular lymphocytic infiltrate; dilated capillaries	Ch. 56
2-Urticarial lesions lasting >24 hours			
<u>Allergic urticarial eruption</u>	Annular edematous plaques; favors trunk	Superficial and deep lymphocytic infiltrate with eosinophils	
<u>Annular erythema of infancy</u>	Recurrent annular erythematous plaques, usually lasting a few days; typically affects infants 3–11 months of age (see Fig. 20.5)	Perivascular lymphocytes and eosinophils	
<u>Wells' syndrome</u>	Edematous erythematous plaques, often annular or arcuate with a greenish color centrally; pruritus; peripheral blood eosinophilia	Diffuse infiltrate of eosinophils; flame figures	Ch. 26
<u>Urticarial vasculitis</u>	Urticarial plaques, often annular, that may have a purpuric component; pain, burning and/or pruritus; systemic manifestations in hypocomplementemic form	Leukocytoclastic vasculitis	Chs 19 & 25
<u>Erythema migrans</u>	Erythema slowly migrates from site of tick bite; influenza-like syndrome; secondary distant lesions	Superficial and deep perivascular lymphohistiocytic infiltrate; eosinophils and plasma cells in erythema migrans; mucin in LE tumidus and annular erythema of Sjögren's syndrome	See text and Ch. 73
<u>Erythema annulare centrifugum (deep)</u> <i>EAC</i>	Annular erythema with raised borders		See text
<u>Lymphocytic infiltrate of Jessner</u>	Annular erythematous plaques; favors face and upper trunk		Ch. 121
<u>LE tumidus</u>	Annular erythematous plaques; favors face, upper trunk > extensor forearms		Ch. 42
<u>Annular erythema of Sjögren's syndrome</u> ¹ <i>SS</i>	Annular erythematous plaques; favors face, arms, upper trunk; most common in Asian patients; anti-Ro antibodies		Ch. 45
3-Granulomatous lesions			
<u>Granuloma annulare</u> <i>GA</i>	Skin-colored to pink annular and arcuate plaques with borders composed of multiple papules; favors acral and extensor sites	Palisading granulomas with altered collagen and mucin	Ch. 92
<u>Annular elastolytic giant cell granuloma</u>	Pink annular plaques with atrophy and hypopigmentation centrally; favors sites of chronic sun exposure	Granulomatous infiltrate with elastophagocytosis by giant cells (border of lesion); absence of elastic fibers (center of lesion)	Ch. 92
<u>Interstitial granulomatous dermatitis (IGD); interstitial</u>	Annular erythematous plaques (or, in IGD, linear cords); favors axillae, groin and	Palisading granulomas surrounding tiny foci of degenerated collagen;	Ch. 45

DIFFERENTIAL DIAGNOSIS OF FIGURATE ERYTHEMA			
Disorders	Clinical features	Histologic findings	Cross references
granulomatous <u>drug</u> reaction (IGDR)	lateral trunk; associated arthralgias/arthritis; IGDR is most often due to antihypertensive and lipid-lowering agents	neutrophils and eosinophils; little to no mucin	
Sarcoidosis	Red-brown annular plaques and papules; favors face; systemic manifestations	Sarcoidal granulomas ('naked tubercles')	Ch. 92
Borderline or <u>tuberculoid</u> leprosy	Annular plaques with raised erythematous borders and (in tuberculoid lesions) central hypopigmentation; asymmetric distribution; hypoaesthesia, alopecia	Linear or oval perineural granulomas in the dermis; foamy macrophages and AFB in borderline lesions	Ch. 74
4-Papulosquamous lesions			
Erythema annulare <u>EAC</u> centrifugum (<u>superficial</u>)	Annular lesions with trailing scale; favors thighs, hips and trunk	Superficial perivascular lymphocytes with focal parakeratosis and spongiosis; focal hemorrhage in pityriasis rosea	See text
Erythema gyratum repens <u>EGR</u>	Concentric erythematous rings with wood-grain appearance; erythema moves \square 1 cm per day; associated with cancer		See text and Ch. 52
Pityriasis rosea <u>P.R</u>	Herald patch on trunk; oval annular papules and plaques with central fine scaling plus a collarette of trailing scale; Christmas-tree distribution on posterior trunk		Ch. 10
Tinea corporis <u>T.C</u>	Annular plaques with scale (exception: tinea incognito); pustules in border; concentric lesions in tinea imbricata; KOH-positive	Dermatophytes in the stratum corneum	Ch. 77
Lichen planus (LP) <u>LP</u>	Violaceous annular plaques; gray-brown to brown hyperpigmentation centrally; mucosal involvement; photodistribution in actinic LP	Hypergranulosis, band-like lymphocytic infiltrate at dermal-epidermal junction, necrotic keratinocytes	Ch. 12
Annular LE (subacute > discoid), neonatal LE, <u>NLE</u> mothers of boys with chronic granulomatous disease	Photosensitivity; favors face (discoid), extensor upper extremities/upper trunk (SCLE), periorbital area (neonatal LE); anti-Ro antibodies (SCLE, neonatal LE)	Vacuolar interface dermatitis; often periaxial lymphohistiocytic inflammation	Ch. 42
Seborrheic dermatitis <u>SD</u>	Erythematous annular plaques with scaling; favors face and central chest	Psoriasiform epidermal hyperplasia, spongiosis, perivascular lymphocytes	Ch. 14
Psoriasis <u>PS</u>	Annular scaly plaques with slow expansion	Parakeratosis, diminished granular layer, elongated rete ridges, neutrophils migrating into epidermis	Ch. 9
Ichthyosis linearis circumflexa of Netherton syndrome <u>Ich</u>	Serpiginous or circinate erythematous plaques bordered by double-edged scale; trichorrhexis invaginata; atopic diathesis, elevated serum IgE	Psoriasiform features	Ch. 56
5-Lesions with absence or variable presence of scale			
Annular lichenoid dermatitis of youth	Red-brown annular patches or thin plaques with central hypopigmentation; favors groin and flanks; affects children and young adults	Lichenoid infiltrate; marked keratinocyte necrosis limited to the tips of rete ridges	
Secondary syphilis <u>24</u> $\frac{1}{2}$	Annular plaques with central hyperpigmentation; favors face; flu-like symptoms; additional cutaneous manifestations; positive for RPR and FTA-ABS	Perivascular and interstitial infiltrate with plasma cells; also lichenoid or granulomatous infiltrate, exocytosis	Ch. 81
Mycosis fungoides <u>MF</u>	Annular erythematous or hypopigmented plaques, some with scale; admixed with classic lesions; often with pruritus	Infiltrate of atypical lymphocytes in the dermis and clustering in the epidermis; also plasma cells and eosinophils	Ch. 120

~8 3-11-2018

Erythema Multiforme (EM)

Key features

- A self-limited but potentially recurrent disease
- Abrupt onset of papular 'target' lesions, with the vast majority of lesions appearing within 24 hours
- Two types of target lesions are recognized: (1) typical, with at least three different zones; and (2) atypical papular, with only two different zones and/or a poorly defined border
- Target lesions favor acrofacial sites
- Has 2 types:
 - ① Erythema Multiforme minor: typical and/or occasionally atypical papular target lesions with little or no mucosal involvement and no systemic symptoms
 - ② Erythema Multiforme major: typical and/or occasionally atypical papular target lesions with severe mucosal involvement and systemic features
- A preceding HSV infection is the most common precipitating factor; occasionally, there are other preceding infections or, rarely, drug exposure
- Diagnosis of erythema Multiforme requires clinicopathologic correlation and is not based solely on histologic findings
- Erythema Multiforme does not carry the risk of progressing to toxic epidermal necrolysis TEN TEN

NB:

Erythema multiforme is now regarded as probably distinct from Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN).

SJS TEN

• Beligra
• Emed
• Dermot
• Fit2 pat.

Erythema Multiforme (EM)

Sudden

def. Acute self-limited & Sometimes recurring skin Condition Considered to be Type IV Hypersensitivity react. (or III) ass. with Certain infections, Medications & other Various Triggers.

Pathophysiology: EM is Considered as Cut. Immune react. That's Triggered by Certain factors in genetically predisposed individuals:

HLA 33
HLA B15, 35
HLA DQW3

• A33
• B15, 35
• DQW3

- A. Genetics:** ↑ incid. of HLA-DQW3 in HAEM & HLA-B15, 35 / HLA33 in recurrent EM
- B. Triggers:** → الجرث

إم 1
إم 2

HSV
Mycoplasma pneumoniae
Drugs
Idiopathic

Idiopathic
HSV
Drug

PRECIPITATING FACTORS IN ERYTHEMA MULTIFORME	
Infections (approx. 90% of cases)	Viral <ul style="list-style-type: none"> ✓ Herpes simplex virus (HSV-1, HSV-2) (50%) <u>HSV</u> • Parapoxvirus (orf) • Vaccinia (smallpox vaccine) • Varicella zoster virus (chickenpox) • Adenovirus • Epstein-Barr virus • Cytomegalovirus • Hepatitis virus • Coxsackievirus • Parvovirus B19
	Bacterial <ul style="list-style-type: none"> • <u>Mycoplasma pneumoniae</u> • Chlamydia (formerly Chlamydia) psittaci (ornithosis) • Salmonella • Mycobacterium tuberculosis
	Fungal <ul style="list-style-type: none"> • Histoplasma capsulatum • Dermatophytes
Drugs (<10% of cases)	Primarily: <ul style="list-style-type: none"> • Non-steroidal anti-inflammatory drugs (<u>NSAIDs</u>) • Sulfonamides • Antiepileptics • Antibiotics
Exposures	<ul style="list-style-type: none"> • <u>Poison ivy</u>
Systemic disease (rare)	<ul style="list-style-type: none"> • Inflammatory bowel disease (<u>IBD</u>) • Lupus erythematosus¹ (Rowell's syndrome) • Behçet's disease¹
Idiopathic	

HSV 2
Mycoplasma pneumoniae
Drugs
Idiopathic

This is a nonexhaustive list based primarily on case reports and small series of cases. The most common causes are in bold.

Pathophysiology: of EM ass:

1- HSV

2- Drugs (DAEM)

Mechanism of herpes associated EM (HAEM) → HL

48 جرة
للإصابة

Herpes simplex (HSV)-associated EM is a delayed type hypersensitivity (DTH) reaction that develops in response to infection in predisposed individuals. The process has been well studied and involves a number of steps:

① HSV infection of keratinocytes, which may or may not result in signs of clinical infection.

CD34+ cell

2. CD34+ cells (Langerhan's precursor cells) transport HSV DNA fragments to distant keratinocytes.

③ HSV gene fragments are expressed in these distant keratinocytes (HSV DNA and HSV-encoded proteins can be detected within the early red papules or the outer zone of target lesions in 80% of individuals with EM and may persist for 3 months after a lesion has healed MAY be due to difficulty clearing the virus from infected cells). However HSV virus cannot be cultured (low level of replication).

HSV

4. This is thought to be followed by an 'autoimmune' response (type 4) resulting from the recruitment of T cells (Th1) that respond to autoantigens released by lysed/apoptotic viral antigen-containing cells → IFN-γ → an inflammatory cascade resulting in the skin eruption of EM.

NB: Drug-induced EM involves a different mechanism with elevated tumour necrosis factor alpha rather than gamma-interferon and CD8+ cells and not CD4+ T helper cells.

TNFα
CD8+

Epidemiology:

Age: any but usually: 20-40 yrs.

Sex: M ± > F.

Race: No predilection.

مستوى
فصل الربيع

Clp:

EM can be divided into:

Types of EM

1. Minor ✓
2. Major ✓
3. Persistent
4. Continuous
5. Mucosal (Myeloplasma)
6. Recurrent (HSV)
7. Bullous
8. Urticarial

CS
IBO
EBV
HSV

EM Minor

• Cut. lesions (Typical Target or papular atypical Target)

X. Absent or mild Mucosal affect

• -ve prodromal (systemic) features

• Healing: 2-3 wks

• MR: 0% X

EM Major

• Cut lesions as Minor ± Bullae.

• Severe Mucosal affect ✓

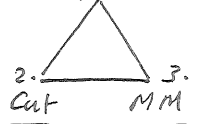
• Moderate prodroma (systemic features)

• 2-6 wks

• <5%

ل. الرتبة

1. Systemic prodroma



(HSV inf.)
↓ 3-14 days



HSV inf.

(Herpes Labialis in 50%)

3-14 days

(وليكه ستن ايدو ستن
الغاري ايدو ستن EM)

1. Prodromal symptoms (systemic manifestations)

→

Absent in EM minor

& Mod. in EM major (50%)

CIP:

Non specific

URT inf. (fever of low

grade, Cough, Rhinitis & arthritis)

duration: ~ 3 ds

3 ds

↓

2. Cut. involvement

Few days Later

MM involvement

Absent or mild in EM minor & severe in Major EM
Site 1-2 mucosal sites are affected

usually 1 oral MM but ± Eye, GIT, Genitalia.

CIP: Hundreds of skin lesions Erupt in

24 hrs of full involvement occurs over 72 hrs.

Lesion start as: well defined

Pink macules → Papules

→ plaques of Target or Papular Atypical Target lesions.

Site → Acrofacial:

L > L.L) - Face & Neck
- dorsal hands & feet

UL > L.L - Elbows & knees (± grouping)

NB. Koebner phenomenon & photo accentuat. may occur

lesions are ass. with

Burning & pruritus

distribution may be:

Linear

Zosteriform

Blaschkoid.

دليل 3

Stomatitis
cheilitis

CIP: Mucosal redness &

swelling → Blisters

→ large, shallow, painful ulcers

Typical

Lips: Swollen & Hgic crust

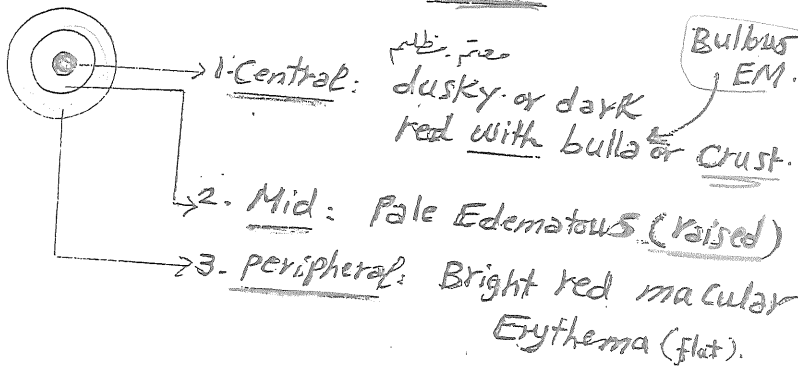
↓
difficult speaking & swallowing

Types of Target lesions

Typical Target (Iris lesion)

Well defined

def. rounded, regular, ≤ 3 cm diameter,
if it is → Palpable with 3 Zones:



Atypical Target ✓ (Targetoid)

def. as Target but formed of 2 Zones &/or poorly defined border.

• Papular
Atypical Target

↓
EM

• Macular (flat)
Atypical Target

↓
SJS/TEN

Course:

① Resolution of EM occurs.

- EM Minor → 2-3 wks
- EM Major → upto 6 wks

Without scarring but \pm dyspigmentation

② Complications (Mucosal)

- usually No Complications except 2ry bact. Inf.
- More \pm EM Major; Includes: Immuno Compromised EM Major.

① Ocular: conjunctivitis, Iritis, Uveitis, Symblepharon & \pm Blindness.

② Oral: difficulty in consuming food → Dehydrat.

③ Genital: (Vaginal & Urethral lesions are rare):
retent., phimosis, Hematocolpus, urethral stricture.

MR — EM minor 22%
EM Major 22% < 5%

Ref.
Cever & Bologna

Histopathology

EM is 1
prototype of
vacuolar form
of
ID.

Dermis

VID with individual KCs (Basal) Necrosis (satellite KCs).
or Apoptosis (ass. with) superficial dermal
Edema & sparse-moderate perivascular Lymphoid
infiltrate.
(CD4 > CD8)
others:
(CD4 > CD8)

epid

- Epidermal spongiosis & Exocytosis.
- Satellite KC Necrosis (intra epid. Lymphocytes attached to Necrotic KCs)

IgM
C3

Immunofluorescence:

Non Specific

- ① granular IgM & C3 around BVs & focally at DEJ
- ② HSV Ags are +ve within KCs by PCR
- ③ HSV genomic DNA can be detected by PCR.

NB: on pathology:

- 1- EM is clinicopathological diagnosis; Not a pure pathologic diagnosis → Histopath. is chic but not specific
- 2- diff. bet. Drug induced EM & HSV induced;

± required to exclude other conditions

TNF-α
CD8

Drug induced (DAEM)

- More KC Necrosis
- More pigment incontinence.

IFN-γ
CD4

HSV induced: (HAEM)

- More Exocytosis & VID
- More upper papillary dermal Edema.
- Nuclear dust in papillary dermis.
- CD4 > CD8

Eosinophils

→ Eosinophils

↑ Acrosyringal

→ Acrosyringal Concentrate

of Apoptotic KCs (clue for ID)

3

CD8 > CD4.
diseases & Necrotic (Apoptotic) KCs:

[FDE
PL

[GVHD
CTDs

[Viral Exanthema
Phototoxic Dermatitis.

DD of EM: (causes of Targetoid lesions): مميز

①. SJS/TEN

• urticaria

• FDE ← Fixed Drug Eruption.

• Vasculitis (e.g. AHEI) Acute hemorrhagic edema

• PND  Paraneoplastic Pemphigus

• EAC → Erythema Annulare Centrifugum

• SCLE → Subacute Cutaneous LE

Diff. bet. EM & Urticaria:-

Table 21.3 --- Differences between urticaria and erythema multiforme.

DIFFERENCES BETWEEN URTICARIA AND EM	
Urticaria	EM
Central zone is <u>normal skin</u>	Central zone is <u>damaged skin</u> (dusky, bullous or crusted)
Lesions are <u>transient</u> , lasting <u>less than 24</u> hours	Lesions ' <u>fixed</u> ' for at least <u>7 days</u>
New lesions appear <u>daily</u>	All lesions appear <u>within first 72 hours</u>
Associated with swelling of face, hands or feet (angioedema) ✓	<u>No edema</u> ✗

Diff. bet. EM & Generalized FDE:

There is clinical & Histopath. overlap.

: علائق تفرق *

من العدد No of lesions at first outbreak

[in FDE → fewer ✓ قليل

[in EM → Hundreds ✓ كثير

Treatment of EM

prophylactic $\uparrow\uparrow$ (For recurrent EM)

- 1- Remove the drug
- 2- Mycoplasma pneum. \rightarrow Erythromycin
- 3- HSV \rightarrow chr. suppressive
For recurrent HREM > 6 ly.
dose: ACV: 10 mg/kg/d in divided doses
(200-400 Twt/d)

durat: 6-12 ms

if failed

- VCV \rightarrow 0.5-1 g/d
- FCV \rightarrow 250 mg/d

Recurrent

ولا مپا: ان صت لرفف لوبيل EM بدون
مروا HSV نط ل ACV لان لعودي مكن
مكون «Sub clinical inf» او نعل HSV
erology

if failed

(Idiopathic EM)

Continuous use of:

- Dapsone
- Antimalarial
- Azathioprin
- Thalidomide
- CYA
- PUVA

Active $\uparrow\uparrow$ (Acute rash)

Symptomatic $\uparrow\uparrow$

- 1- Itching \rightarrow oral antihistamines & Topical Cs
- 2- oral pain \rightarrow mouth washes
Containing anaesthetics & Antiseptics
- 3- Eye \rightarrow ophthalmologist.

For

EM minor EM Major
تعالج البيت
 \downarrow
Hospitalizat.

4

هل نطفي
Cs
ولا لا؟؟

- Its use is controversial
as it \pm \uparrow risk of
infectious complications

يس لوهانطها يبق بشرطين:

- 1- Early initiat
- 2- Severe dis

(Give)
prednisolone or
pulse Mp.

STEVENS-JOHNSON SYNDROME AND TOXIC
EPIDERMAL NECROLYSIS (SJS/TEN)

Key features

- Prodrome of upper respiratory tract symptoms, fever and painful skin
- Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are two rare, potentially fatal adverse cutaneous drug reactions of differing severity characterized by mucocutaneous tenderness and erythema as well as extensive exfoliation
- SJS is characterized by <10% body surface area of epidermal detachment, SJS-TEN overlap by 10-30%, and TEN by >30%
- The medications most frequently incriminated are antibiotics, non-steroidal anti-inflammatory drugs, and antiepileptics. TEN and SJS usually occur 7-21 days after initiation of the responsible drug
- The average mortality rate is 1-5% for SJS and 25-35% for TEN; it can be even higher in elderly patients and in those TEN patients with a very large surface area of epidermal detachment
- Exfoliation is due to extensive death of keratinocytes via apoptosis; the latter is mediated by interaction of the death receptor-ligand pair Fas-FasL
- Optimal medical management of SJS and TEN requires ¹early diagnosis, ²immediate discontinuation of the causative drug(s), and rapid initiation of ³supportive care and specific therapy
- Specific therapies that have the potential to selectively block keratinocyte apoptosis, such as high-dose IVIg, may provide added benefit over supportive care alone

Stevens Johnson Syndrome & Toxic Epidermal Necrolysis

(SJS/TEN)

def. SJS/TEN is a very rare, acute serious & potentially fatal skin reaction in which there is sheet-like skin & mucosal loss usually caused by medications.

Cause: usually Drug induced:

① 200 drugs can cause SJS/TEN (so any drug can cause SJS/TEN unpredictably).

② Risky drugs:

• Drugs with longer half-lives

• Most common drugs:

• Sulfonamides (Septin®)

• Allopurinol

• NSAIDs (Oxicam type)

• Anticonvulsants

✗ ③ Risky Patients:

• HIV why??

→ Use of Sulfonamides
→ atypical pattern of production or detoxification of drug metabolites

• GVHD

• CTDs

Drugs that most commonly cause SJS/TEN

Antibiotics Antifungals Antivirals	<ul style="list-style-type: none"> • Sulfonamides, e.g., cotrimoxazole; beta-lactams i.e., penicillins, cephalosporins • Imidazole antifungals • Nevirapine (non-nucleoside reverse-transcriptase inhibitor)
Allopurinol	
Nonsteroidal anti-inflammatory drugs (NSAID) (oxicam type mainly)	<ul style="list-style-type: none"> • Naproxen • Ibuprofen
Anti-convulsants	<ul style="list-style-type: none"> • Carbamazepine • Phenytoin • Phenobarbital

• valproic acid

• Lamotrigine

Pathophysiology

→ unknown but 2 Mechanisms were proposed:

1- Genetic Mechanism:

A. Patients \bar{e} SJS/TEN & Their 1st degree relatives may have genetic defects that → accumulation of Toxic Metabolites of The drugs.

For example: Patients \bar{e} Sulfonamide-induced TEN have been shown to have Slow acetylator Genotype → ↑ products

of sulfonamide hydroxyl amine (via P450 Pathway) which is a Toxic Metabolite that → TEN

← Via either: ① Direct toxic effects or ② Hapten Mediated Mechanism → break Self Tolerance to Endogenous proteins.

↓
Perforin Mediated KCs apoptosis

B. ↑ in cid. of HLA B12:

in Allopurinol induced TEN → HLA B5801

in Carbamazepine ~ ~ → HLA B1502

2 Interaction bet. Cell surface death receptors:

(Fas-FasL Mechanism): The interaction bet

Fas & Fas-Ligand → apoptosis. this interaction can be blocked by IVIg → stop of dis. progression \bar{e} in 1-2 ds \bar{e} No mortality.

What is perforin??

making mono-mc

granules re-

from NK

cells →

The Target

forming po-

rs & Tubular st-

ures (not unlike

Attack Complex

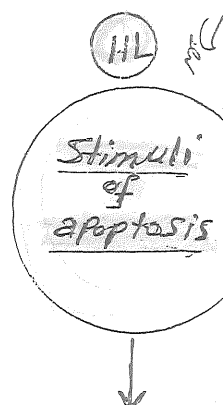
plement

+

?

Receptors:
CD95)
Cell death
receptors

Fas ligand is
a membrane
member
of TNF
member



1. Cellular stress.
2. Growth factor withdrawal
3. DNA damage
4. Cytokines release (TNF)

↑ FasL Expression by KCs & localized Extracellularly

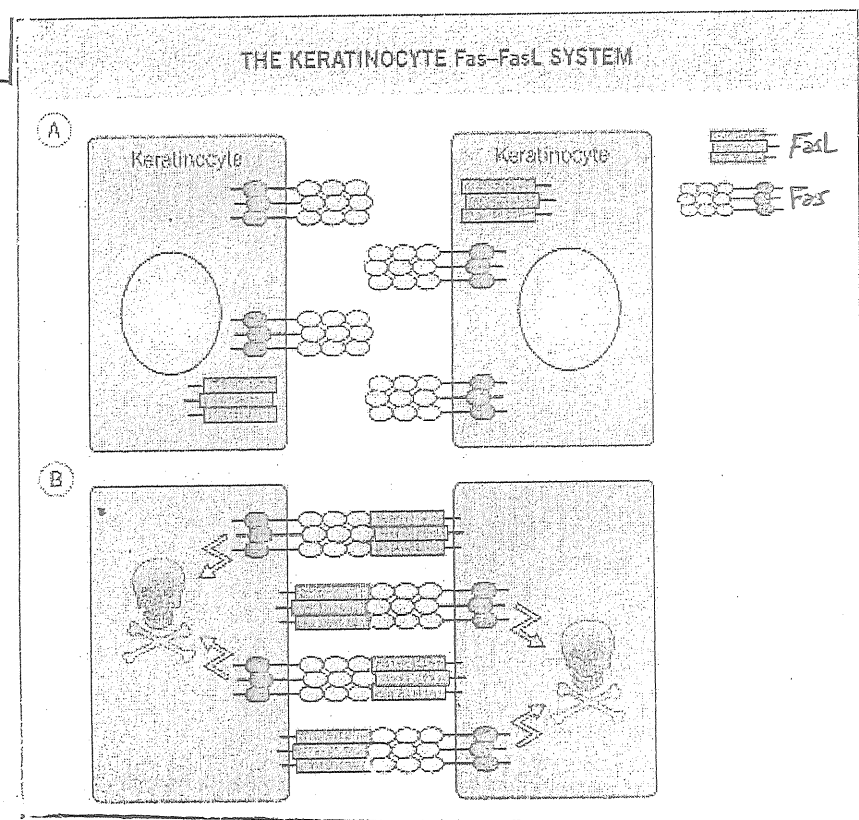


Fig. 21.5 The keratinocyte Fas-FasL system in normal skin and its role in toxic epidermal necrolysis (TEN) and treatment with IVIg. A In normal skin, low levels of Fas ligand (FasL) are expressed by keratinocytes and localized intracellularly. B In lesional skin of TEN, high levels of FasL are expressed by keratinocytes and localized on the cell surface. Upon contact with Fas, cell surface FasL induces Fas multimerization and rapid signaling leading to keratinocyte cell death by apoptosis.

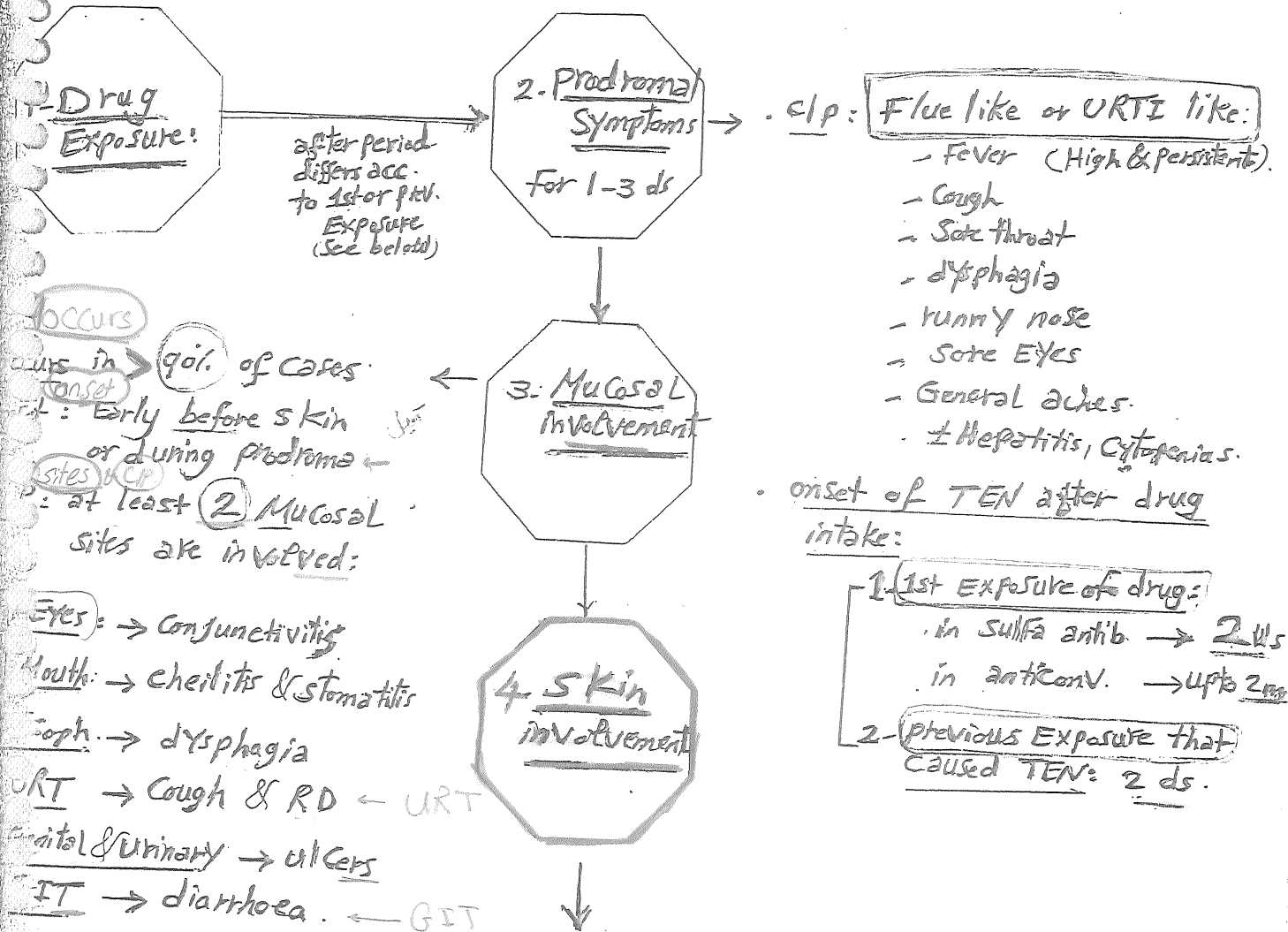
initiation of Fas Signaling
Pathway of Apoptosis

Fig. 21.4 The Fas signaling pathway of apoptotic cell death. The death receptor Fas and its ligand FasL are transmembrane proteins. Fas signaling is triggered in the target cells by receptor tri(multi)-merization, induced upon contact with membrane-bound Fas from an adjacent cell. Subsequently, recruitment of intracellular signaling proteins FADD and pro-caspase-8 leads to activation of the protease caspase-8 as well as apoptosis due to subsequent activation of downstream effector caspases (caspases-3, -6, -7), which cause cellular disintegration and death. Stimuli that induce apoptosis include cellular stress, growth factor withdrawal, DNA damage and cytokines.

Epidemiology:

- Age: any but common in **46-63** (d.t. ↑ drug intake)
- Sex: M:F = 1:1.5.
- Race: any

CIP:



They are Very Tender

• **Early** (3) + B1

• usually: **Macules**: Erythematous, dusky red or purpuric

• May be: **Targetoid** (flat Atypical Target)
• **Scarlatiniform**

• These lesions ch-By:

• Very Tender & Painful

• show (+ve) pseudo-Nikolsky sign

• **Late:**

Large flaccid fluid filled blisters → Epid. detachment with exposure of underlying dermis or is raw & bleeding (scalded)

• (+ve) Asboe Hansen sign.

Epid. → wet Cigarette Paper
Dermis → scalded

Sites of skin involvement:

- Start on the Trunk & extends rapidly to face & Limbs (sp. photosensitive & Trauma sites).
- distal legs & arms: relatively spared but palmo-plantar areas may be an early sites of involvement (bullae will be Tense??)

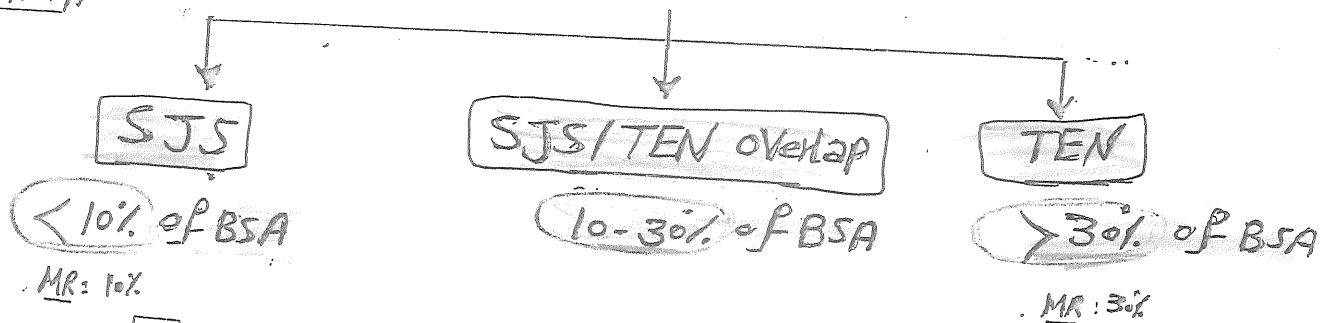


After diagnosis of SJS/TEN clinically
you have to do 2:

Note

detached ←
or
detachable
(By Nikolsky)

A Classification of the patient: based on extent of skin detachment.



B Assess severity & predict the out come by: SCORTEN

Table 21.6 -- Scorten.

SCORTEN	
Prognostic factors (7)	Points
Age >40 years	1
Heart rate >120 bpm	1
Cancer or hematologic malignancy	1
BSA involved on day 1 above 10%	1
Serum urea level (>10 mmol/l)	1
Serum bicarbonate level (<20 mmol/l)	1
Serum glucose level (>14 mmol/l)	1
SCORTEN	
	Mortality rate (%)
0-1 → 3	3.2
2 → 15	12.1
3 → 30	35.8
4 → 60	58.3
=5 → 90	90

BSA → Body surface Area

ارتفاع تقریباً

NB Healing occurs by epithelialization from NL surrounding skin & form H. Follicles (No need for Graft).

Complications of SJS/TEN

Toxic Epidermal Necrolysis

This condition can be fatal due to complications in the acute phase. The mortality rate is up to 10% for SJS and at least 30% for TEN.

A-During the acute phase, potentially fatal complications include:

- Dehydrate
- Malnutrition
- Infect → Skin MM - pneumonia ✓
Blood → Septicemia ✓
- DIC & MOF.

B-Longterm complications include:

- ① Skin: Dyspigment & Scarring (at pressure areas & dt Inf)
- ② Nails: pterygium & dystrophy.
- ③ Joint: Contractures.
- ④ Genitalia:
 - phimosis.
 - vaginal synchiae.
 - ulcers.
- ⑤ Eye:
 - conjunctivitis.
 - Keratitis → opacities & ulcers.
 - Symblepharon → adhesion bet Eye lid & Eye ball
 - Ectropion or Entropion.
 - Trichiasis → Inverted Eye lashes.
 - Synchiae → bet Iris & Cornea.

⑥ Cause of death

- ① inf (sp ^{staph &} Pseudomon.)
- ② fluid loss & Elect. imbalance
- ③ Insulin loss or ↓ response.
- ④ Hypercatabolism.

- ① inf
- ② fl
- ③
- ④

INVS. of SJS/TEN

- 1 Lab:
- ① CBC
 - ② chemistry profile
 - ③ LFTs
 - ④ RFTs

- ⑤ PT
- ⑥ APTT
- ⑦ Culture of Blood & denuded areas.

- 2 Rad:
- 1- Baseline radiograph: d.t frequent Tracheobronchial involvement & RD
 - 2- GIT: radiograph to detect effects

confirm
D.
Exclude
other dis
SSS
AGEP

3 Histopathology:

Early Lesions

- ① KC Necrosis (scattered (individual) Apoptotic KCs in basal & suprabasal layers)

This correlates with the dusky to gray color of lesions

والى اول ماضوفا علامته
ان لونه هادي خلع

Full-blown Epid. Necrosis.

Late Lesions

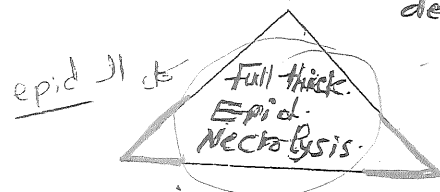
subepid.
Blisters with

overlying confluent

- ① Necrosis of entire Epid. + spaler

- ② Perivascular Lymphocytic infiltrate of papillary dermis.

Spaler



Note

Lymphocytes of:

Epid.: CD8+ & Macrophage

Dermis: CD4+

CD8+
CD4

CD8
CD4

Blister at granular layer

Neutrophilic infiltr. Epid. pustules

DD of SJS/TEN

- الاصفر ←
- EM
 - SSSS
 - AGEP ←
 - Generalized FDE → Fixed drug eruption
 - other:
 - PNP → Paraneoplastic Pemphigus
 - LAD
 - LE → Lupus E
 - Kawasaki
 - Acute GVHD Graft versus Host disease

1. EM → Typical Target Lesions
- .. affect Face & Extremities

↓
see table

حالة الاضرار
التي فيها
Targeted
lesions

.. Also see table of diff. of EM.

2. SSSS

- Etiology → Staph. aureus Exotoxin (Epidermolyisin) → attack DSG1
- Age: → usually Newborn & Young children
.. adults may be affected if: R For Immunosuppressed.
- No MM or PP affection.

Nikolsky sign is (+ve) & fragile bullae are (+ve) but they lead to: Exfoliat leaving bed of intact epidermis (instead of scalded dermis of TEN). dit difference in level of separation. ??

✓ Nasal discharge → frequently present
 • Histopath. → see before.

3 AGEP:

def. Adverse cut. Drug reaction ch by large areas of erythemas studied \bar{e} small ($< 3mm$) "non" follicular pustules. MM → 20% & Nikolsky sign \pm ve.

← chicallly → Neutrophilia
 Eosinophilia
 pustules all are against TEN

4. Generalized FDE:

- Multiple Mucocut. affect \bar{n} may occur.
- overlap clinically & histologically may occur \bar{e} SJS.
- determinat \bar{n} of No of lesions during 1st (Fewer) out break may be useful (بداية التفريق)

5- Others: ... Le

• PNP, LABD, GVHD → clinical & Path. criteria (\bar{e} + ve IF).

Note Vancomycin → commonest drug causing LABD ... uncommon cause of TEN.

• Kawaski: No conj. Exudate
 PP & perioral → epid. split
 No Targetoid lesions.

TEN Like Vesiculobullous lesions seen in Patient e SCL&SLE may occur & called

((ASAP Synd.))

« Acute synd. of ^{pan}apoptotic x Epidermolysis »

(Acute synd of Apoptotic pan epidermolysis)

Treatment of SJS/TEN
(Hospitalizatⁿ)

IVIG + Supportive

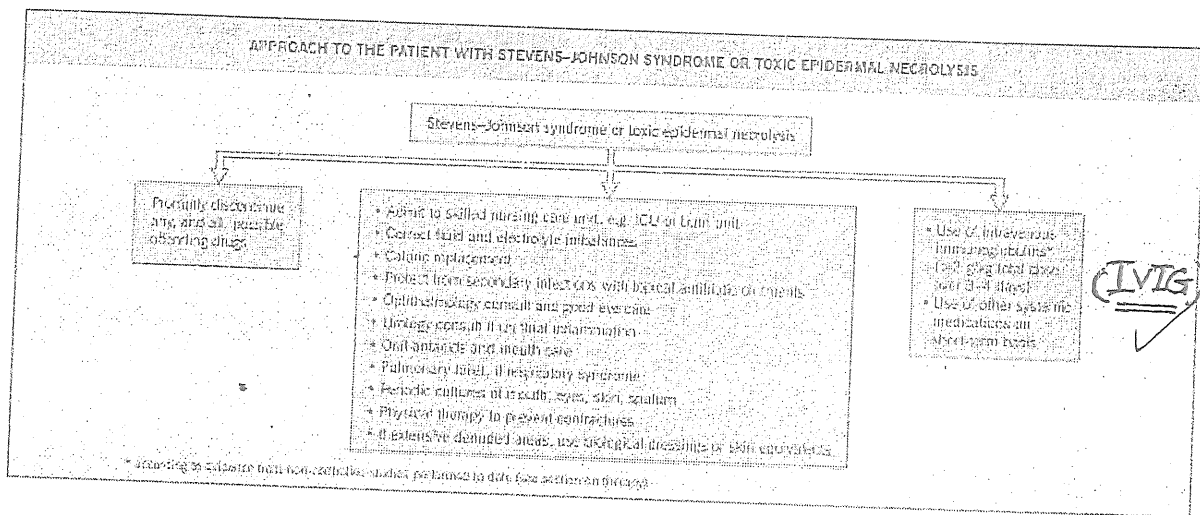


Fig. 21.13 Approach to the patient with Stevens-Johnson syndrome or toxic epidermal necrolysis.

1. ICU or burn unit.
2. Correct Fluid & Electro Imbalance
3. Caloric intake
4. Topical Antib.
5. Mouth Care
6. Eye Care (بناغ)
7. Urological Care (شالوك)
8. Joint Care (علاج مفاصل)

IVIG → Cyclosporine [أفولاديسين]

NB. Role of CS: Controversy but may be used in short courses (Pulses)

✗ Thalidomide: a Voided (TMR)

Cyclosporine: 3-4 mg/kg/d

Cyclophosphamide: 100-300 mg/d

N-acetylcysteine: 2g/6hrs

Avoid → Thalidomide

IVIG → 1g/kg/d for 3 consecutive days

Diff. bet: SJS / TEN

9

	EM	SJS / TEN
<u>Cause</u> <u>Age</u> <u>Sex</u>	<u>(Inf.)</u> (HSV) - 20 - 40 Ys. - (M) > F	- <u>Drugs</u> . - > 46 Y - (F) > M
<u>prodroma</u> <u>Skin:</u> <u>A. site:</u> <u>B. lesion:</u>	<u>Absent - moderate</u> <u>Acrofacial</u> ① <u>plaques, Target or papular atypical Target</u> . ② <u>± Bullae</u> (EM Major) ③ <u>No</u> epid. detachment < 10%.	<u>Severe</u> ✓ <u>Trunk then extends</u> ^{Face} _{Neck} . <u>Macules, flat atypical Target</u> <u>Bullae</u> <u>Epid. detachment</u> <u>> 10%</u>
<u>BSA</u> <u>MM:</u> <u>onset</u> <u>No</u> <u>Severity</u>	<u>Skin</u> ^{بشرة} _{أخضر} <u>Common</u> but <u>mild</u> - <u>Mod. usually only</u> <u>oral</u> (1 <u>Mucosal site</u>) <u>absent</u> . ✗	<u>Skin</u> ^{بشرة} _{قبل} . <u>Severe</u> , involving at least (2) <u>Mucosal sites</u> (2-3). <u>Not frequent</u>
<u>Int. organs affected</u> <u>Duration</u> <u>Complications:</u> <u>MR</u>	<u>2-6 wks</u> , <u>No</u> ✗ <u>0% - < 5%</u>	<u>> 2-6 wks</u> . <u>(±) Complicated</u> (أشياء) <u>10-30%</u> ↑
<u>Pathology</u> <u>##</u>	<u>VID with individual KC Necrosis & stellites</u> <u>Sparse-mod. papillary dermal Lymphoid infilt</u> <u>± Edema</u> . <u>CD4</u> > CD8 <u>See EM</u> <u>prophylactic AcV</u> → <u>active</u> _{sympt + Cs}	<u>Subepid. Blisters</u> <u>± Full thickness</u> <u>Epid Necrosis & sparser</u> <u>Lymphoid infilt.</u> <u>CD8</u> > CD4 <u>See SJS/TEN</u> <u>IVIG</u>

Target-
± Bullae
No detachment

من
من
من

Intravenous immunoglobulin

Sub
(all sources) ← B cells, Dendritic, T, DNNT, EMed, T

Definition: Intravenous immunoglobulin (IVIG) is a sterile solution of globulins extracted from the pooled plasma of about 10,000 to 20,000 individuals.

(mostly IgG ± IgA)

Mechanism:-

① Immuno-suppressive: (-- Complement Mediated damage & block Fc Rs on surface of Macrophage & B-cells)

② Anti-inflammatory: ↓ inflammatory mediators (cytokines, chemokines, metallo-proteinases)

③ Anti-microbial: ↓ circulating pathogens.

④ Its recent success in treating TEN is believed to be a function of its ability to inhibit apoptosis. Theoretically, IVIG acts as a Fas (CD95)-blocking antibody, inhibiting Fas: Fas ligand-induced keratinocyte death.

XX (FAS, FAS-L)

⑤ NB- In persons with Kawasaki disease and dermatomyositis, IVIG is thought to inhibit the generation of membrane attack complexes (C5b-C9) and subsequent complement-mediated tissue damage by binding the activated components C3b and C4b, thus preventing their deposition on target surfaces.

Indications:

IDP
ITP
Leuk
HIV
Immune
GVHD
Kawasaki

(A) FDA approved indications: 7 conditions: (1 to 8)

- ① Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- ② Immune Thrombocytopenic Purpura (ITP)
- * ③ Primary immunodeficiency states eg. Iry and X-linked agammaglobulinaemia.
- ④ Chronic Lymphocytic Leukaemia
- * ⑤ Paediatric type-1 HIV
- ⑥ Kawasaki syndrome (ang)
- ⑦ Prevention of Graft vs. Host disease in adult bone marrow transplant recipient

(The first four conditions account for 70% of IVIG use)

(B) Non FDA approved indications (offlabel uses): → see table:-

(TEN, DM, AD, Bullous dis, PG)

Dosage & Administration:

تحديد الجرعة في الوريد على مدار 2-4 ساعات في يوم أو يومين أو أربعة

1 - 2 g/ml/kg in 500-1500 ml saline or glucose (IV) infusion over 2 hrs for 2-4 ds. every 4 wks (4 weeks) then tapered to every 2-4 ms.

High doses

in inflamm & imm. dis.

في مرة واحدة على يومين أو أربعة

تأثيرات الجراحة تباعد لدرجة

NB: in Kawasaki dis: single 2g/ml/kg over 12hs → effective.

2g/ml/kg
ساعة
12

How long do the effects of IVIG last?

The duration of the response from IVIG depends on the individual's metabolism and the disease state. On average, the effects of IVIG can last up to a month after each administration.

Contraindications:

1-Absolute:

History of hypersensitivity to IVIG.

(IV IG)

to Thimerosal

(Thimerosal)

IgA deficiency (Deficiency of IgA occurs in about 1 in 700 of the population and should be screened before IVIG therapy is instituted)

لا يتم اختبار

IgA

2-Relative:

RF & HF (↑ risk of fluid overload).
RA & cryoglobul (↑ risk of RF).
pregnancy (C)

Side effects: IVIG is generally well tolerated. Most side effects are mild and self-limited.

A-Common side effects (within 30-60mins) → Vasomotor

خلال ساعة

- Flushing.
- Urticaria
- Headache
- Chills
- Fever
- Nausea or vomiting
- Wheezing
- Lower back pain
- Tachycardia (rapid heart beat)
- Changes in blood pressure

FAHM

HR

Bp

✓ Myalgia (muscle pain)

These symptoms can be managed by stopping the infusion or a patient can be premedicated with antihistamines and intravenous hydrocortisone.

B-Rare side effects:

Ⓜ: Topical & Systemic CS

ARF ⑥ Acute renal failure (most common after use of sucrose-containing products which can cause an 'osmotic nephrosis')

Blood → Blood clots
Haemolysis
Neutropenia

skin → skin reactions:

① Blistering eczema is the most common (a type of dermatitis). It often begins at about 8 to 10 days after exposure to IVIG. The rash characteristically begins as a dyshidrotic eczema (pompholyx) but this may be followed by a more generalised eczematous eruption that spreads throughout the body (The affected individual may become erythrodermic (red all over) and pruritic (itchy))

onset: 8-10 days

② Urticaria

③ Maculopapular rash

④ Lichenoid eruption (like lichen planus)

⑤ Diffuse hair loss

⑥ Cutaneous vasculitis

Drug interact? No interact but the live attenuated Vaccines (LAV) may ↓ its efficacy.

disadvantage: Cost, ≈ 30,000 LE / cycle

③: ① Risk of infection from IVIG: The pool of donors is carefully screened to eliminate anyone with abnormal liver function or exposure to viral hepatitis or HIV infection. The process of obtaining IVIG itself removes viruses and bacteria from the plasma. Therefore, IVIG should not pose any risk of hepatitis C, hepatitis B or HIV transmission. Since the introduction of newer techniques of obtaining IVIG in 1987, there have been no cases of transmission of these viruses.

What happens upon re-exposure to IVIG? When an individual develops a skin reaction to IVIG, a second exposure may cause the rash to appear earlier (generally around 8-10 days after infusion) and be more extensive. This is because the immune system has developed memory T-cells and subsequent responses are faster and more severe. Switching the type of IVIG may cause a less severe reaction.

الاسماء التجارية:

- Gammagard S/D (Baxter/Hyland; Deerfield, Ill)
- Gammar-IV (Armour; Blue Bell, Pa)
- Gamimune-N (Miles; Elkhart, Ind; Bayer)
- Iveegam (Immuno-US; Rochester, NY)
- Polygam S/D (Baxter/Hyland for American Red Cross; Washington, DC)
- Sandoglobulin (Sandoz; Vienna, Austria)
- Venoglobulin-I or Venoglobulin-S (Alpha Therapeutic; Los Angeles, Calif)
- Carimune/Panglobulin (ZLB Bionasema/ABC Swiss Red Cross)

FLUSHING

غشال استخوان

- Emed.
- Betignia
- DNNZ
- RCK

nic.
d.
nt
mb
dne.
s/s

11y

Introduction:

Flushing is the term used to describe transient and episodic reddening of the skin, most commonly of the face, and less often the neck, ears and upper chest.

Table 106.2 -- Causes of flushing.

CAUSES OF FLUSHING

1- **Physiological:** as part of normal thermoregulation in response to :

- ✓ Exercise
- ✓ Hot drinks
- ✓ Hot environment
- ✓ Blushing (emotionally triggered.. حمرة الخجل)

2- **Exogenous agents:**

• Alcohol

الخمر

• Drugs

- * Angiotensin-converting enzyme (ACE) inhibitors **ACEI**
- * Calcium channel blockers **CCBs**
- * Calcitonin
- * Chlorpropamide¹
- * Cholinergic agonists (e.g. pilocarpine)
- * Cyclosporine
- * Disulfiram¹
- * Fumaric acid esters (ttt of PS. → ttt by trental as it -TNFα)
- * Gold ('nitritoid reactions')
- * Hydralazine
- * Nicotinic acid ← **smoking** ← الدخين
- * Nitrates (e.g. glyceryl trinitrate)
- * Opiates
- * Prostaglandins **PGs**
- * Sildenafil, tadalafil, vardenafil **Viagra**
- * Tamoxifen

• Foods

- ✓ Spoiled scombroid fish (التونا والماكاريل الفاسد) → flush, sweating, vomiting, diarrhoea due to histamines (لوعاوز تشخصه قيس هيستامين البول)
ttt → H1,2 blockers, Cs, Epinephrin.
- Spicy food (gustatory flushing. ass. with sweating).

• Foods additives

- Monosodium glutamate (MSG), sodium nitrite, sulfites

3- Menopause (80% of menopausal). **[Hot Flashes]**

غشال

4- Neurologic disorders :

NB Acral Flushing

- Erythema Ab Igne.
- Erythromelalgia
- Post Raynauds

1 Acral Flushing

→
→
→

order
of
treat
ment
in
flushing

Why

3-4-2

CAUSES OF FLUSHING

- ✓ Anxiety
- ✓ Autonomic dysfunction
- ✓ Tumors (e.g. hypogonadal pituitary tumors)
- ✓ Migraine
- ✓ Frey's syndrome (auriculotemporal syndrome)

5- Systemic diseases

- Carcinoid syndrome
- Mastocytosis
- Pheochromocytoma
- Medullary carcinoma of the thyroid
- Thyrotoxicosis
- POEMS syndrome
- Pancreatic tumors (e.g. VIPomas)
- Prostaglandin-secreting renal cell carcinoma

→ Urine: 5 H.I. Acetat (Serotonin Metabolite)

→ Urine: Vanillylmandelic acid

2 thyroid

6 cut: Rosacea. 7 Idiopathic

Pathogenesis

Flushing is caused by relaxation of dermal
BVS w. may be mediated by either:

① Autonomic Nervous system → Flushing + Sweating
(Wet Flush)

② Vasoactive Mediators → Flushing (without) Sweating
(Dry Flush).

Table 44.2 Causes of flushing.

(Mediators of V. relaxat-)

Cause	Proposed mediator(s)
Physiological	Autonomic
Menopausal	Autonomic
Drug induced	Various
Alcohol	Acetaldehyde
Chlorpropamide and alcohol	Acetaldehyde
Food	Autonomic
Scombroid fish poisoning	Histamine
Carcinoid syndrome	Serotonin Prostaglandins Bradykinin Histamine
Mastocytosis	Histamine
Thyrotoxicosis	Thyroxine
Medullary carcinoma of the thyroid	Prostaglandins Calcitonin
Pancreatic tumours	Vasoactive Intestinal peptide
Insulinoma	?

Complications:

① Blushing → anxiety & embarrassment

② Fixed Erythema, Telangiect & Rosacea.

DD ① Burning Sensat- + Erythema

AICTDs, photo damage, photo sensitivity.

② Rosacea ??

- ① Remove underlying Et → Menopause (ERT)
- ② Idiopathic → clonidin, BB, anxiety → anxiolytic
- ③ Menopausal → clonidin, SSRIS, ERT³
- ④ Blushing → psych. Anxiolytic, clonidin

⑤ resistant cases → surgical

NB Paroxetine is FDA For Menopausal Flushing

Paroxetine